**DATA AND SAFETY MONITORING PLAN**

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## A. Protocol Summary

### A1. Brief protocol description.

In the context of an NIH R34 grant, we previously developed and pilot tested, Keep It Up! (KIU!), an online HIV prevention program tailored to ethnically diverse young men who have sex with men (YMSM; 18-24 years old). KIU! is based on the Information-Motivation-Behavior Skills (IMB) model of HIV risk behavior change and informed by principals of E-learning. Our small-scale pilot randomized clinical trial (RCT) demonstrated the feasibility and acceptability of the KIU! intervention: we enrolled an ethnically diverse sample of YMSM; achieved excellent retention through 3-month follow-up (89%); maintained robust intervention engagement; and produced a significant 44% decrease in unprotected anal sex relative to an active control. The current study is a two-group, active-control, RCT of KIU!. The overarching goals are to advance scientific knowledge of technology-based, behavioral HIV prevention, as well as improve public health by establishing the efficacy of an innovative eHealth prevention program for YMSM. We will accomplish these goals with three specific aims.

*Aim 1: Integrate the KIU! intervention into a widely-used health technology platform to increase its scalability, adaptability, and potential for broad implementation.* We will spend the first 6 months of the project collaborating with in house computer scientists to integrate KIU! into a technology platform developed as part of the NIH Roadmap to integrate electronic assessment into clinical research and care[9-12]. This also includes programming of a new booster session and an improved tracking interface.

*Aim 2: Test the efficacy of the KIU! eHealth intervention in a multisite RCT that meets CDC criteria for "best evidence interventions"[13].* To do this, we will:

a) Enroll ethnically diverse YMSM (N = 900; > 65% racial/ethnic minorities) who tested HIV negative from the clinics of our community partners in Chicago, Atlanta, and New York. The majority of participants will be those who engage in substance use prior to sex. We anticipate that approximately 4500 YMSM will have to be screened to enroll this number of YMSM.
b) Randomize participants to either the highly interactive and engaging KIU! intervention or an HIV knowledge condition similar to existing web-based HIV educational materials.
c) Measure intervention outcomes through 12 months post-intervention. The primary behavioral outcome will be the count of unprotected anal sex acts and the primary biomedical outcome will be STI incidence. Additional behavioral outcomes include: alcohol and drug use prior to sex, risky sex after substance use, condom errors, IMB factors, and receipt of an HIV test. We will test for dose effects and decay in intervention effects over time.

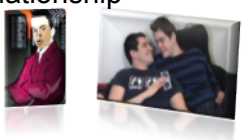
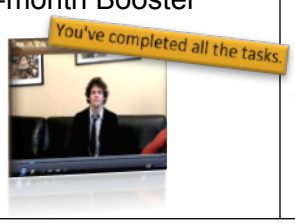
*Aim 3: Explore if the KIU! intervention has differential efficacy across important sub-groups of YMSM.* We will explore moderators of intervention effects by testing for significant differences in the magnitude of intervention effects based on the types of substances used prior to sex, as well as race/ethnicity, relationship status, and gay/bisexual identity. These findings will be used to assist in future targeting of KIU! delivery and identify need for further intervention tailoring.

### A2. Study design.

This is a two-group, active-control, RCT of KIU!, an online intervention. Participants will be randomized to two groups in equal proportions (KIU! condition n=375; control arm n=375). The KIU! intervention involves 7 modules completed across three sessions (See Table 1 for module descriptions),done at least 24 hours apart (i.e., at least 3 days), and totaling ~2 hours to content. An innovative aspect of KIU! is that each module is based on a particular setting or situation relevant to the lives of YMSM, with developmentally appropriate health behavior change content embedded within each of these settings. Module content is designed to be

sensitive and responsive to user bandwidth. Across these modules, the KIU! intervention uses diverse delivery methods (e.g., videos, animation, games) to address gaps in HIV knowledge, motivate safer behaviors, teach behavioral skills, and instill self-efficacy for preventive behaviors. The control condition contains the same number of modules as the KIU! condition, with the same requirement to participate across three sessions. It reflects HIV information that is currently available on many websites so as to understand how the KIU! intervention improves upon what is currently available online. It is didactic, not tailored to YMSM, non-interactive, and focused on HIV/STI knowledge. Using this approach as a control condition will ensure that both groups have equivalent access to the Internet for HIV-related content. Booster sessions will be delivered at 3 and 6 months for each arm.

**Table 1: KIU! module descriptions.**

| *Module* | *Style* | *Content* |
|---|---|---|
| 1. Healthy and Whole Person  | Diverse peer videos | Welcomes and engages participants in the intervention. Discusses connections to family, community, and romantic partners and setting positive peer norms for condom use and obtaining support from family of origin and choice[68,69]. |
| 2. Hooking up Online   | Stylized animation with 3 scenarios | Follow three YMSM chatting online with a focus on identifying triggers for unprotected sex. Embedded content focuses on the effects of mood on risk[137,138], negotiating correct condom use, consequences of drug and alcohol on decision making[19], and facts about STI symptoms and prevention. |
| 3. Sex in the City  | Scripted soap opera style video | A diverse cast of YMSM highlight the risks in making assumptions about a partner's HIV status or monogamy, the limits of serosorting in HIV negative YMSM when only ~20% of HIV+ YMSM know their status[139], the importance of regular testing, and skills for negotiating condom use within relationships. |
| 4. The Club   | Virtual reality game | Through interactive game play, participants address pros/cons of condom use, steps to correct condom use, consequences of excessive alcohol consumption or drug use, issues with presuming HIV status in others, and effects of sexual arousal on decision making[19]. |
| 5. Dating (an Older Partner)  | Flash animation quiz style | Explores the power dynamics between an older and younger man in a dating relationship, and how YMSM can assert healthy behaviors[95]. Embedded in the module is identification of a continuum of safer sex behaviors and strategies for implementing them. |
| 6. A Serious Relationship  | Illustrated story with flash and scripted scenarios | An illustrated story about dating and considers ways to get sexual, emotional, and health needs met in relationships and how ongoing condom use can be an important aspect of that. The module also includes a video of a YMSM who receives an HIV diagnosis while in a relationship. It wraps up with a video with actors portraying examples of good and bad communication about condom use. |
| 7. Setting Risk Reduction Goals  | Prevention goals worksheet | Participants develop a realistic and practical HIV and STI prevention plan. Suggested goals are tailored to risks reported in participants' baseline assessment data. The purpose is to plan to prevent previous risky behaviors and to troubleshoot obstacles to successful implementation of the plan. |
| 3-month Booster   | Scripted and loosely scripted video and animation | A chance to revisit goals, receive tailored feedback to troubleshoot obstacles, and set new goals or re-affirm existing ones. Included is a series of videos that follow a new character after he has a HIV scare and learns the importance of regular HIV testing and condom use. Also included is video follow-up from one of the characters from the Module 3 soap opera who, like the participants, received an HIV negative test result in the recent past and is working to maintain his risk reduction as |

| | | |
|---|---|---|
| | | some of the fear accompanying the test has subsided (delivered at 1.5 months in pilot KIU! trial, now at 3 months). |
| 6-month Booster | Loosely scripted videos, animation, and game scenarios | A chance to revisit goals, receive tailored feedback to troubleshoot obstacles, and set new goals or re-affirm existing ones. Included is a series of videos that follow the character introduced in the 3 month booster as he navigates the dating scene and becomes involved in a serious relationship. The character learns the importance of having a partner who meets his emotional, physical, and health needs. Also included is information on stopping and restarting condom use in a relationship. They are links to review content from the original intervention modules. |

**A.3. Primary and secondary outcomes.**

The primary behavioral outcome will be the count of unprotected anal sex acts and the primary biomedical outcome will be STI incidence. Additional behavioral outcomes include: alcohol and drug use prior to sex, risky sex after drug use, condom errors, IMB Model factors, and receipt of an HIV test. Similar procedures and measures successfully used in the developmental study will be employed (study measures are described in Table 1). Assessments will be completed via the Internet using a Computer-Assisted Self Interview (CASI). We will administer knowledge/information based measures immediately post-intervention along with the measures of intervention acceptability and tolerability. Motivation, skills (i.e. partner sexual communication, correct condom use), and behavioral outcomes (i.e. number of insertive and receptive unprotected anal sex acts, condom errors) will be measured at all follow-up points. Whenever possible, we selected measures: (1) designed for high-risk YMSM to maximize sensitivity, (2) previously tested with diverse populations to minimize cultural bias, and (3) to maximize comparability to other studies in order to compare findings.

**Table 1: Study measures.**

| | **Construct**<br>Administration Points | **Measure** |
|---|---|---|
| Primary Outcomes | Unprotected sex acts HIV testing, and substance use<br>BL \| \| 3 \| 6 \| 12 | The AIDS-Risk Behavior Assessment (ARBA)[191,192] has been used with YMSM[82,102,191] and assesses behaviors on a partner-by-partner level, starting with recent partners, as well as in the aggregate. Partners are classified as serious or casual and relationship duration is measured[95]. Questions differentiate between insertive and receptive anal sex. The ARBA will also assess drug and alcohol use, and secondary outcomes of HIV testing behaviors. |
| | STI incidence<br>BL \| \| 3 \| 6 \| 12 | CT and GC testing of urine and rectal samples using the FDA cleared Gen-Probe APTIMA Combo 2 Assay. All participants will be tested at baseline and 12 month follow-up. Participants who test positive at baseline will also be tested at 3 month and 6 month follow-ups.. |

| | | |
|---|---|---|
| Secondary Outcomes | HIV Information<br>BL \| \| 3 \| 6 \| 12<br>Motivation & Behavioral Skills<br>BL \| \| 3 \| 6 \| 12 | *The brief HIV/AIDS Knowledge questionnaire assess knowledge of transmission and prevention [193]. It has strong internal consistency, test-retest stability[193], and has been used successfully with young adults[194]. A total correct score will be used in analyses.<br>*HIV/AIDS Motivation and Behavioral Skills[195] assesses: Motivation (e.g. intentions to use condoms, perceived threat of HIV or STI infection, motivation to become safer), Social Norms (e.g., partners, friends, or family members opinions about condom use), and Behavioral Skills (e.g. self-efficacy, negotiating condom use). Internal reliability alphas range from .73 to .94 and the measure has been used and developed for MSM. *Behavioral skills also include: the Condom Errors Questionnaire[196], that assesses condom use errors within the last 3 months (e.g. using oil-based lubricant). The scale has been found to be predictive of condom breakage and slippage[197,198] and has been used with YMSM[199,200].<br>*The Health Protective Communication Scale measures how respondents discuss health protection with their sex partners. It has been used with diverse adolescent and young adult samples (alpha = .84 in a national sample[201]). |
| Other Measures | Intervention acceptability and tolerability<br>\| Post \| \| \| | Developed by Tarnowski and Simonian[140], it includes a combination of open-ended questions (e.g. "What aspect of the program did you like the least?") and closed-ended Likert-style questions that form a scale of intervention acceptability (alpha = .87). |
| | Dose, engagement, and process<br>During Intervention | Intervention dose will be defined as the number of module and booster sessions completed. Although time logged into the intervention will be tracked, it is a poor proxy for engagement as individuals may stay logged in even when not engaged and a "time out" function only partially rectifies this. To measure engagement we will track key activities within modules (e.g. interactions within games) and develop a score based on participant deviations from sample average engagement. We will include measures related to the process of the intervention, such as the environment where participants complete the modules (i.e. location, level of privacy, etc.) and reasons for non-participation in the study; and at the end of each assessment we will ask participants if they have experienced any adverse events as a result of their participation in the study (see Human Subjects). |
| | Demographics and reading ability<br>BL \| \| \| \| | We will use standard measures of age, ethnicity, education, and socio-economic status. YMSM-specific items include gender identity, sexual orientation identity, and anatomic sex at birth. Reading ability at or above an 8th grade level will be assessed during the screening questionnaire using an adaptation of portions of the Peabody Picture Vocabulary Test-Revised used successfully in the R34 [202]. |

We have created a short exit interview script to collect qualitative data from participants after they complete their final 12 month follow-up assessment. We will conduct 20 exit interviews by phone to hear participants' thoughts on the intervention and its effect on their behavior. Ten participants will be randomly selected from a pool of intervention completers who responded well to the intervention (defined as a reduction in condomless anal sex acts at 12-month follow-up) and ten participants will be randomly selected from a pool of intervention completers who did not respond well to the intervention (defined as no change or an increase in condomless anal sex acts at 12-month follow-up). By including people who did versus did not respond well to the interview, we will be able to better understand differences in participants' experiences that may have contributed to whether or not the intervention changed their behavior. We will record the interviews by putting the call on speakerphone mode and using a handheld digital recording device. Before beginning the exit interviews, the study team will ask participants for verbal confirmation that they agree to complete the exit interview and have the conversation recorded. Participants will be reminded that all of the information they provide during the exit interview is confidential and that they can refuse to answer any questions that they do not feel comfortable answering. The study team will transcribe the audio and review responses for feedback on the intervention. The information gained from the qualitative interviews will be used to continue to refine the intervention in future iterations. It will also help the study team to understand whether or not participants find it acceptable to complete and return biological samples for STI testing, which will inform future research efforts. The interview will take 10 – 15 minutes to complete and participants will be compensated with a $5 gift card as thanks for their time and participation.

**Repeat STI Interviews:** Preliminary data analysis indicates that a subset of KIU participants tested positive for rectal STIs more than once during the study. We plan to continue refining the KIU program in future research, so we are interested in getting a better understanding of what factors are contributing to repeat STIs in this subset of participants. This information will allows us to add content to future iterations of the intervention to address these issues and hopefully reduce the occurrence of repeat STIs in this population. In order to gain this important information, we have created a brief interview script to collect qualitative data from 20 randomly selected participants from a pool of participants who tested positive for rectal STIs more than once during the study. We will conduct interviews by phone to learn about participants' experiences getting tested for and seeking treatment for rectal STIs, including their reactions to testing positive for a rectal STI, how it influenced their thinking and behavior, and their experiences related to seeking treatment (e.g., barriers to seeking treatment, doctors' reactions). We will record the interviews by putting the call on speakerphone mode and using a handheld digital recording device. Before beginning the interviews, the study team will describe the potential risks and benefits associated with participating in the interview, describe how we handle privacy and confidentiality, and ask participants for verbal consent to participate in the interview and to have it audio recorded. Participants will be reminded that all of the information they provide during the interview is confidential and that they can refuse to answer any questions that they do not feel comfortable answering. The study team will transcribe the audio and conduct qualitative data analyses in order to identify themes in responses. The information gained from the qualitative interviews will help to broaden our understanding of risk for repeat rectal STIs, including identifying factors that may be barriers to accessing treatment. This information has the potential to inform future development of HIV/STI prevention interventions for this population. The interview will take 10-15 minutes to complete and participants will be compensated with a $10 gift card as thanks for their time and participation. Participants who are difficult to reach (defined as non-responsive to 3 contact attempts) will be offered a $20 gift card as thanks for their time and participation. Participants who are recruited for these interviews come from a relatively small subset of participants who tested positive for rectal STIs more than once during the study, so we hope increasing the incentive for difficult to reach participants will help us reach our goal of 20 interviews. Increased incentives like this have been shown to increase participation among difficult to reach and non-responsive participants in other research studies without perceptions of coercion.

**Timed Post-Release Testing:** We will use time spent on intervention and booster sessions as a proxy for participant engagement and as a means to refine future implementations of KIU!. In order to determine a baseline measurement for the amount of time it takes to complete each intervention and booster session, we will recruit 20 participants via online social media and application ads. We are recruiting participants who meet the same eligibility requirements as the 900 participants who were enrolled into the KIU! intervention. Potential participants will click the ad, fill out a screener, and, if eligible, provide contact information. They will then be contacted by a KIU! study staff who will describe KIU! in greater detail. If they are still interested in participating in the timed post-release testing, a research assistant will email potential participants a link to an online consent form. Once the participant has consented, a research assistant will email them a unique link to the first intervention session. Participants will be given ten days to complete the three intervention sessions and 3- and 6- month booster sessions. After participants complete the 6 month booster session, study staff will call participants to complete a 10 – 15 minute exit interview. Participants will be reminded that the conversation will be recorded, all of the information they provide during the exit interview is confidential, and that they can refuse to answer any questions that they do not feel comfortable answering. The study team will transcribe the audio and review responses for feedback on the intervention. The information gained from the qualitative exit interviews will be used to continue to refine the intervention in future iterations. Overall, participants will spend approximately 2 hours and 45 minutes completing study activities (2 ½ hours for the online intervention and booster sessions, and 10 – 15 minutes for the phone exit interview). Participants must complete the intervention, two booster sessions, and phone exit interview to be mailed a physical $50 Visa gift card.

Our approach to the distance STI testing follows Co-I Sullivan's effective protocol for the Checking In Study. To test for STIs, we utilize at-home urine collection kits and at-home rectal swab test kits which both use the FDA approved Gen-Probe APTIMA Combo 2® Assay[204], a target amplification nucleic acid probe test that utilizes target capture for the in vitro qualitative detection and differentiation of ribosomal RNA from CT and NG. Gen-Probe reports sensitivity of 98 – 100% and specificity of 98 - 100% for urethral CT and NG. Urine

and rectal samples will be tested in the Centers for Disease Control and Prevention (CDC) Division of STD Prevention Laboratory.

STI testing protocol at baseline will vary based on enrollment site. Participants who enroll off-site (e.g. at home or at a library) will be shipped both test kits in a nondescript box. Easy-to-understand instructions for collecting and returning the samples will be provided with the kits. In addition to the written instructions provided with the rectal STI kit, a private video with instructions for properly collecting the rectal samples will be shared with participants. The sample collection kits are identified by study ID only. After the samples are returned through the mail and processed by the CDC lab, results will be sent on at least a biweekly basis to Northwestern University via secure email. If a specimen is not received within 3 weeks of mailing, an electronic reminder will be sent through the medium chosen by the participant (text message or email) or phone if no preferred medium was selected by the participant. Repeat reminders will be sent in subsequent weeks if the specimen remains unreturned and, eventually, telephone follow-up will be used to support participants whose specimens were overdue by 4 weeks from time of mailing. The STI testing protocol at all follow-ups will be the same for these participants.

Participants who enroll on-site at Emory University, Hunter College, or Northwestern University will collect samples for STI testing while at the university site. Easy-to-understand instructions for collecting and returning the samples will be provided with the kits. In addition to the written instructions, KIU! staff will be on hand to address any concerns or questions that participants have about self-administering the test kits. The sample collection kits are identified by study ID only. KIU! staff will mail the STI test samples to the CDC. After the samples are returned through the mail and processed by the CDC lab, results will be sent on at least a biweekly basis to Northwestern University. For these participants, the STI testing protocol at all follow-ups will be the same one used by participants who completed their baseline STI testing off-site.

In most cases, participants who are recruited on-site at a CDPH clinic will have already completed STI testing as a part of their clinic visit. CDPH clinics also test for STIs using the FDA approved APTIMA assay. Participants who have already completed STI testing will be asked to consent to the clinic's UIC lab sharing their results with study staff via fax. It typically takes 3 – 7 days for the return of results. CDPH staff will be responsible for providing these participants with treatment and reporting positive results to appropriate authorities. During instances in which a client has not already completed STI testing or declines to consent to the clinic's UIC lab sharing their test results, university staff will offer the client the option to take the test kits home, be mailed the test kits by university staff, or self-administer the test kits while still on-site at the CDPH clinic. Participants who self-administer at home will be responsible for mailing the kits back to the CDC for analysis. Participants who self-administer on-site at the CDPH clinic will have their kits mailed by university staff to the CDC for analysis.

All STI results will be manually entered into the study's REDCap tracking database. In order to avoid data entry errors and sharing incorrect results with participants, the study team will do comprehensive checks on logged results and the PDFs of results sent to participants (see "F.3.e.(i). Data handling, transmission, and storage" for more details).

If a participant's specimen is positive, the Physician of Record at the CDC reviews the results before releasing to participants. We will deliver test results to participants using a secure, encrypted email. To open the email and access their results, participants must enter the Study ID that was provided to them with their test kit. They will be able to download and print out a hard copy of their results. Participants may speak to research staff if they wish. With positive test results for chlamydia or gonorrhea, research study staff will provide local referrals for free or low cost treatment and make a legally required confidential report to the appropriate health department. STI testing and results will also be self-reported at behavioral assessment time points throughout the follow-up period to determine if a participant tested positive and was treated prior to the 12-month STI test.

Participants living abroad at the time of their 12-month STI test will be encouraged to visit a local healthcare provider to get tested for chlamydia and gonorrhea. The study team will not mail at-home STI test kits to participants living abroad due to high postage costs. If participants do not know where to get tested, study staff

will help them find local, free or low cost healthcare providers offering urethral and, whenever possible, rectal STI testing. The study team will also attempt to refer participants to LGBT friendly healthcare providers if available nearby. Participants who get tested in this manner will be emailed and asked to complete an "Authorization for Release of Medical Records" form that allows their healthcare provider to share their STI test results with the study. The authorization form notes that participants can revoke their authorization to share their health information with the study team at any point. Participants will be instructed to sign the authorization form, scan or take a high quality photo of the form, and email it back to the study team. Upon receipt of the authorization form from the participant, study staff will request the participant's STI test results via secure, HIPAA compliant fax from the healthcare provider.

**A.4. Inclusion/exclusion criteria.**

We will include participants in the study if they: (1) MSM, defined as a birth male who identifies as male and who self-reports having sexual contact with another male in the past year; (2) received an HIV negative test result from a participating clinic/recruitment site or from at-home HIV testing; (3) are 18-29 years old; and (4) had unprotected anal sex with another male in the last 6 months. YMSM will not be enrolled in the study if they: (1) do not have an e-mail address that can be used to contact them for retention purposes; (2) are currently in a behaviorally monogamous relationship lasting longer than 6 months. We use this criterion because we believe safer sex interventions for MSM in long-term monogamous relationships will require substantial tailoring from those who are single or in the early phases of a relationship; (3) did not have unprotected anal sex with another male in the last 6 months. Consistent with recommendations for assuring sufficient event rates in RCTs, this will ensure that sufficient rates of sexual behavior are occurring at pre-test to allow us to detect intervention effects on behavior at follow-up; (4) HIV positive serostatus at time of enrollment. We have elected to exclude HIV+ individuals because we believe that secondary prevention messages may need to be different than primary prevention messages. Nevertheless, if a participant seroconverts during the course of the study, he will be allowed to continue participating (with appropriate adjustment in the analyses). We will also refer him for HIV services; and (5) since the measures and intervention are delivered in English, participants must be able to read English at a minimum 8$^{th}$ grade level.

**A.5. Power calculation and sample size.**

All power calculations were performed in R version 2.14.0 and using common sample size formula for repeated measures[210] with nominal Type I error rates (i.e. α=.05) and effect estimates based on our preliminary studies. We will screen approximately 4500 YMSM, enroll 900 YMSM, and assume 80% retention based on our preliminary studies. Assuming participants are randomized to two groups in equal proportions (KIU! condition n=375; control arm n=375), we will have 97% power to detect a 11% reduction in the rate of unprotected sex (ERR = 0.89) due to the intervention, assuming the correlation between repeated measures is 0.8. The correlation among repeated measures plays an important role in the calculation; in this case, our power calculation is conservative if the correlation among repeated measures is, in fact, weaker than 0.8. The smallest effect size with which we will have 80% power to detect is a 6.5% reduction in the rate of unprotected sex. Technically speaking, our study will have greater power than what is reported here after we adjust for our blocked design. In conclusion, we will have 80% power to detect an effect size equal to half of what we observed in our pilot trial and less than half of the lower bound of effect sizes seen in other HIV prevention programs with MSM[26]. For our primary biomedical endpoint of STI incidence, we assume the annual incidence based on our longitudinal cohort studies in the range of 10 to 15%. If the incidence rate in the control group is 10%, we will have 81%, 70%, and 56% power to detect an incidence reduction of 7%, 6%, and 5%, respectively. If the incidence rate in the control group is higher, say 15%, then the power reduces to 71%, 60%, and 47%, respectively. The objective of aim 3 is to estimate the intervention effect among subgroups and test for significant differences. In data analyses, this will be achieved by testing 2-way interactions, treatment by subgroup. For a conservative power calculation, we repeated the power calculations as per aim 1 with a reduced sample size. Assuming N=200 per group (say, for racial/ethnic subgroups), an ERR=0.89 as above, and strong correlation among repeated measures (i.e. 0.8), we will have 91%, 85%, and 77% power to detect a 10%, 9%, and 8% reduction in the rate of unprotected sex among YMSM, respectively, due to KIU! intervention. The power will be less for effect sizes more subtle than 8% and less for smaller subgroups. In addition to racial/ethnic subgroups, other subgroups of interest include sexual orientation identity groups (81%

gay, 17% bisexual identified) and relationship groupings (30% recent serious relationships). The power for each subgroup comparison will be similar to the power described above.

**B. Trial Management**

**B1. List of participating enrolling clinics or data collection centers.**

This interdisciplinary and multisite project requires participation of multiple institutions in order to accomplish the aims of the project. Recruitment of the requisite sample of diverse YMSM and the aim to understand the generalizability of the intervention across diverse settings requires the participation of institutions in multiple cities. The Chicago site will be led by the Principal Investigator (PI), Dr. Brian Mustanski, at Northwestern University (NU) in Chicago, IL. The following community-based organizations (CBOs) in Chicago will be participating in recruitment of participants: Center on Halsted, Broadway Youth Center and Howard Brown Health Center, and Vida/SIDA (a project of the Puerto Rican Cultural Center). The New York site will be led by Co-Investigator, Dr. Jeffrey Parsons, Professor at Hunter College of the City University of New York (CUNY) and the founder and Co-Director of Center for HIV/AIDS Educational Studies and Training (CHEST) of Hunter College. The following CBOs in New York will be participating in recruitment of participants: Gay Men of African Descent, Gay Men's Health Crisis, Hispanic AIDS Forum, Harlem United, and Callen Lorde Community Health Center. The Atlanta site will be led by Co-Investigator, Dr. Patrick Sullivan, Associate Professor at Emory University. The following CBOs in Atlanta will be participating in recruitment of participants: AID Atlanta, AID Gwinnett, and Someone Cares.

**B.2. Projected timetable.**

Our proposed project seeks to advance public health by testing the efficacy of an innovative HIV prevention program for a high risk and underserved population (YMSM) and advance scientific understanding of how to utilize eHealth solutions to reduce HIV/STI risk behaviors and link eHealth intervention to clinical encounters. To achieve Aim 1, months 1-6 will be spent programming new booster content (for 3 and 6 months post-intervention) and conducting technological upgrades in order to bring it to scale in the Northwestern University Assessment Center (AC) platform. To achieve Aim 2, in months 7-54 we will have to screen approximately 4500 YMSM to enroll ethnically diverse young MSM (N=900; >65% racial/ethnic minorities) that test HIV negative from the clinics of our community partners in Chicago, Atlanta, and New York. We will randomize participants to either KIU! or the existing HIV knowledge control condition similar to existing web-based HIV educational materials. We will measure self-report intervention outcomes at baseline and follow-up assessments at 3, 6, and 12 months and STIs at baseline and 12 months. Months 55-60 will be dedicated to analyses and dissemination. We will test for dose effects and decay in intervention effects across the 12 months of follow-up data. To achieve aim 3, we will explore moderators of intervention effects, including race/ethnicity, relationship status, and sexual identity. Table 3 describes the projected timetable for project activities.

**Table 3: Project timeline by 6-month intervals.**

| | Year 1 | | Year 2 | | Year 3 | | Year 4 | | Year 5 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 - 6 | 6-12 | 12-18 | 18-24 | 24-30 | 30-36 | 36-42 | 42-48 | 48-54 | 55-60 |
| Hire Personnel | | * | | | | | | | | |
| Purchase supplies and equipment | | * | | | | | | | | |
| Meeting of Investigators | | | | | | | | | | |
| Multisite meeting with CBOs | | | | | | | | | | |
| Technological upgrades to KIU 1.0 | | * | | | | | | | | |
| Programming of additional booster sessions and recruitment staff training materials | | | | | | | | | | |
| Final usability testing of all modules | | | | | | | | | | |
| Training of multi-site team | | * | | | | | | | | |
| IRB approval | | * | | | | | | | | |
| Recruitment of sample (N in cells) | | 450 | 660 | 660 | 660 | 1035 | 1035 | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Longitudinal Tracking of Sample | | | | | | | | | | * |
| Analysis of trial outcomes | | | | | | | | | | |

**B.3. Target population.**
We will screen approximately 4500 YMSM to enroll an ethnically diverse sample of YMSM between the ages of 18 and 29 (N= 900). Participants will represent an equal proportion of Black, Latino, and White YMSM, consistent with both high-risk YMSM populations in each city, as well as the demographics of the population seeking services at each recruitment site. The majority of participants will be those who engage in substance use prior to sex. Based on our KIU! pilot data, over 50% of YMSM reported drug and/or alcohol use before sex. The team in each city has assembled a cadre of CBOs whose indigenous staff will recruit YMSM upon a negative HIV test result. We have partnered with CBOs for recruitment in order to maximize our ability to test the intervention under conditions in which it would eventually be disseminated.

**(B.3.a.1) CBO Recruitment.** At the conclusion of their post-test appointment or rapid-test, YMSM who test HIV negative will be given a tablet computer by clinic staff (with paper-and-pencil option if preferred). Clients can be screened online on the Assessment Center platform or offline on the iFormBuilder app. The tablet (or paper form) will display information about the study, ask the potential participant whether or not he wants to consider participation, and ask demographic questions for screening purposes. If the participant is not interested, the tablet (or paper form) will ask questions assessing reasons for non-participation. This will allow us to test for potential biases in enrollment. For participants who are determined to be eligible, the device will ask for contact information. For participants who are determined to be not eligible, the device will display ineligibility information and ask the participant if he would like to enter his contact information for consideration in future studies. When paper and pencil are used, participants will provide their contact information if they are interested in participating in Keep It Up! or other studies; they will not be aware of their eligibility at the time. The tablet (and paper form) includes a question in the contact information section asking for consent to add participants to the IMPACT database. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected on the tablet through Assessment Center will be securely uploaded to the tracking system. Information collected on the tablet using the iFormBuilder app will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff. Information collected with paper and pencil will be manually entered by research study staff into Assessment Center within 3 days of receipt. This procedure allows for rigorous tracking of recruitment and participation rates in a timely manner. YMSM interested in participating will be instructed to expect an e-mail with more information about the study and offered local sources of private Internet access if they do not have their own. The Project Coordinators based at Northwestern, Hunter, and Emory will be on hand to provide ongoing training and support to testing staff to assure easy compliance with this recruitment procedure. Brief videos, FAQs, and flow charts will be provided to testing staff to train them on the recruitment procedures.

Potential participants will be sent a recruitment e-mail to the address entered into the tablet. Non-response to the recruitment e-mail after 4 days will trigger the retention protocol that will include two further e-mails, phone calls if a valid phone number was provided, and a text message (if consent provided). Following recommendations for Internet-based research, inclusion criteria will not be posted, but instead measured directly, in order to reduce potential for participant deception in order to gain incentives.

Upon enrollment, participants will be randomly assigned by the online program to receive KIU! or the HIV knowledge control arm. Randomization will be stratified by race and CBO at baseline by computerized system. Stratifying by race will assure sufficient representations by race/ethnicity in each condition to address Aim 3 (exploring potential racial/ethnic differences in outcome effects). Stratification by CBO will prevent imbalance in factors that may influence intervention responsiveness across cities and clinics. After the pre-test assessment and remote STI testing are completed, participants will receive the intervention content across three sessions across a minimum of 3 days and a maximum of 3 weeks, based on principles of effective HIV interventions and high acceptability in the pilot phase. Booster sessions will be delivered at 3 and 6 months.

**(B.3.a.2) Expanded Recruitment.** Recruitment from the CBOs will be supplemented by ads, street outreach, referrals of participants from ongoing studies and participants who have consented to being added to IRB approved research participant registries at the university sites, referrals from the Chicago Department of Public Health (CDPH) clinics, and referrals of participants from community partners who provide HIV testing. In addition to the CBO sites, Emory University and Hunter College will offer HIV testing to participants recruited through these expanded recruitment methods. Participants who visit these university sites will be tested by trained research staff and will join the study in the same way they would if they were testing at a CBO.

Staff members across all testing sites will be trained in appropriate and ethical methods of recruiting participants in medical settings. To minimize the risk for coercion, the staff member and the study information sheet/screen emphasize the optional nature of participation and that it will not affect, in any way, their access to healthcare services. These recruitment procedures were previously approved by the IRBs at the University of Illinois at Chicago, implemented in the KIU! pilot study, and no adverse events were reported.

Northwestern University and Emory University will also offer at-home HIV testing to participants recruited through these expanded recruitment methods. Staff members across all testing sites will use the skills taught during their HIV testing and counseling training to help participants cope with any distress related to their test results. When necessary, staff members will work with the participant to link them to care and will be available to provide counseling support following established organizational procedures.

1. **Recruitment through online, print, and telephone ads.** The KIU! research assistants will place online recruitment ads on popular sites such as Facebook, Grindr, and Craigslist. Additionally, RAs will send private messages to young men on Facebook who “like” or “share” the ads that we post on Facebook. These messages will encourage the young men to click the link in the ad and to complete our online screener if they have not already done so. Samples of the messages we will use are included in the “Recruitment-Online & Telephone Ads samples 5.1.14” document. The RAs will also place recorded recruitment ads on phone party lines like Talkee’s Chicago Blade line where YMSM can chat real time in a group or one-on-one or leave personal ads for being contacted privately. Print ads will be created by the study RAs and distributed to partner CBOs as well as handed out at events where the study target population is in attendance. Participants recruited through these ads will be directed to a study webpage for detailed project information and a brief eligibility screener. Interested participants will provide contact information (name, phone, email address) and complete the screener.

   For those who screen ineligible, the online screener will ask the participant if he would like to consent to enter his contact information for consideration in future studies. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected from the online screener will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff within 3 days of receipt.

   For those who screen eligible, the participant will be asked to confirm his HIV negative status by (1) taking an HIV test at a partner CBO testing site or university site (Emory and Hunter) or (2) taking an at-home HIV test provided by a university site (Emory and Northwestern).

   Participants that agree to take an at-home HIV test will be mailed an FDA approved at-home test kit. Participants will be offered the option of testing with Oraquick (oral swab) or Home Access (finger stick). Before participants are mailed either kit, study staff will call participants to confirm that they are interested in completing at-home HIV testing and collect their mailing address. Once participants have confirmed their interest, study staff will email them a link to the online consent addendum hosted on the secure REDCap website. Kits will be mailed out once the participants indicate their consent to take the test and share results with the study team.

   To join the study with an Oraquick at-home HIV test, participants will be required to interpret their test result by comparing their test stick to the pictures and descriptions on test kit

directions. On the same day that their kit is mailed out, study staff will email or text participants a link to a secure REDCap data collection webpage hosted on Northwestern University servers. After determining their test result, the participant will need to upload a picture of their test stick to the REDCap webpage. The photo that participants upload will only be of the test stick. Participants are not being asked to photograph themselves with the test stick. Study staff will store images of the test sticks linked to the participant's unique study ID on a secure university shared drive for three months. This timeframe will allow participants up to three months from the date they tested HIV negative to fully enroll into the study. If a participant does not have a camera equipped mobile phone or computer with a webcam to take the photo and upload it to the secure REDCap page, participants can call study staff and report their test result.

To join the study with a Home Access at-home specimen collection kit, participants will be required to mail back their blood specimen to Home Access for testing. Participants must use the pre-paid and pre-addressed envelope provided by Home Access to return their blood sample. After shipping their blood specimen, participants will call a toll-free number after seven days to receive their test results and post-test counseling. Participants will also be asked, during the online screener, to consent to allowing Home Access to share their results with research staff. HIV results will be shared between Home Access and Northwestern University via SFTP. University staff will use this information to confirm participants' eligibility for the study.

Participants who agree to take either at-home HIV test kit will also be mailed at-home urethral and rectal STI test kits.

***For individuals with HIV negative test results.***
(a) At CBO sites: The testing counselor will provide the participant with a tablet (or paper form) to complete the full screener and confirm eligibility. If eligible, an enrollment email with a link to the study to be sent to the participant's email address.

If ineligible, the tablet (or paper form) will ask the participant if he would like to consent to enter his contact information for consideration in future studies. When paper and pencil are used, participants will provide their contact information if they are interested in participating in Keep It Up! or other studies; they will not be aware of their eligibility at the time. The tablet (and paper form) includes a question in the contact information section asking for consent to add participants to the IMPACT database. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected on the tablet through Assessment Center will be securely uploaded to the tracking system. Information collected with paper and pencil will be manually entered by research study staff into Assessment Center within 3 days of receipt.

(b) At university sites (Emory and Hunter): The testing counselor will provide the participant with a tablet (or paper form) to complete the full screener and confirm eligibility. If eligible, an enrollment email with a link to the study to be sent to the participant's email address. The testing counselor will encourage the participant to complete the baseline assessment and first set of self-administered STI test kits at the university site. Upon completion, the participant will be compensated $50 in cash.

If ineligible, the testing counselor will also let the participant know that he is ineligible for KIU! but may be eligible for other studies. If interested in other studies, university staff will collect additional contact info using the tablet (or paper form) to enter into the IMPACT database. The participant will also receive $10 in cash for his travel to the university site.
(c) At-home HIV testing: If the participant tests negative, the project coordinator will call the participant to do a full screening over the phone and confirm eligibility. If eligible, an enrollment

email with a link to the study to be sent to the participant's email address. Upon completion of the baseline assessment, the participant will be compensated $30 in Citi Visa gift cards.

If ineligible, the project coordinator will let the participant know that he is ineligible for KIU! but may be eligible for other studies. If the participant is interested in other studies, the project coordinator will collect additional contact info and to enter it into the IMPACT database. All subjects will have to consent to being added to the IMPACT database.

***For individuals with HIV positive test results.***
(a) At CBO sites: The testing counselor will work with the participant to link them to care and will be available to provide counseling support following established organizational procedures. Linkage-to-care will include referring the participant to a clinic that will conduct a free confirmatory HIV test, and to someone that will work with them receive treatment if their confirmatory test returns positive. The testing counselor will also let the participant know that the KIU! research assistant will follow-up with them about their eligibility for the study.

At the conclusion of the appointment or rapid-test, the testing counselor will call the KIU! research assistant and confirm that the participant has tested positive. The KIU! research assistant will email the participant to let him know that he is ineligible for KIU! but may be eligible for other studies. If the participant is interested in other studies and consents to being added to the IMPACT database, the KIU! research assistant will collect additional contact information from him.

(b) At university sites:
Emory – The testing counselor will use the skills taught during their HIV testing and counseling training to help participants cope with distress after receiving a positive test result. The testing counselor will work with the participant to link them to care and will be available to provide counseling support following established organizational procedures. Linkage-to-care will include referring the participant to a clinic that will conduct a free confirmatory HIV test, and to someone that will work with them receive treatment if their confirmatory test returns positive. Participants under 24 years old will be referred to the Ponce de Leon center at Grady while those who are 24 years and older will be referred to their county health department. After the participant has been linked to care, the testing counselor will give the participant $50 in cash for travel and time spent being counseled and linked to care. The testing counselor will also let the participant know that he is ineligible for KIU! but may be eligible for other studies at Emory.

Hunter – The testing counselor will use the skills taught during their HIV testing and counseling training to help participants cope with distress after receiving a positive test result. The testing counselor will work with the participant to link them to care and will be available to provide counseling support following established organizational procedures. Linkage-to-care will include referring the participant to a clinic that will conduct a free confirmatory HIV test, and to someone that will work with them receive treatment if their confirmatory test returns positive. Participants may be referred to the Mount Sinai Comprehensive Health Program, Callen-Lorde Community Health Center, or Gay Men's Health Crisis Prevention Center. The testing counselor and a senior staff member will walk or take a cab with the participant to the HIV confirmatory testing clinic. Before taking the trip to the confirmatory clinic, the testing counselor will give the participant $50 in cash for travel and time spent being counseled and linked to care. The testing counselor will also let the participant know that he is ineligible for KIU! but may be eligible for other studies at Hunter.

(c) At-home HIV testing: If the participant tests positive using an Oraquick test kit, the project coordinator will work with the participant to link them to care and will be available to provide counseling support. The project coordinator will use established organizational linkage-to-care

procedures that have been used in other IRB approved studies. Linkage-to-care will include referring the participant to a clinic that will conduct a free confirmatory HIV test, and to someone that will work with them to receive treatment if their confirmatory test returns positive. In Atlanta, participants under 24 years old will be referred to the Ponce de Leon center at Grady while those who are 24 years and older will be referred to their county health department. In Chicago, participants will be referred to a linkage-to-care specialist at Center on Halsted. In New York, participants may be referred to the Mount Sinai Comprehensive Health Program, Callen-Lorde Community Health Center, or Gay Men's Health Crisis Prevention Center. For participants who live outside of Atlanta, Chicago, and New York, study staff will use the AIDS.gov service locator to make referrals to the nearest health care provider.

If the participant tests positive using a Home Access specimen collection kit, trained counselors employed by Home Access will provide counseling support and linkage to care. Trained study staff at the university sites can provide additional support and linkage to care as necessary.

University staff will be responsible for immediately reporting positive HIV test results to the appropriate health department.

2. **Recruitment through street outreach.** Prior to recruiting through street outreach, the research team will obtain permission from management or owners of venues to recruit for study participants. Once permission is granted, university staff and interns will approach potential participants in various venues that cater to YMSM (e.g. bars, clubs, bathhouses, and festivals), briefly explain the purposes of the study, and invite them to answer questions that screen for preliminary eligibility. Individuals will answer questions privately on a tablet (or paper form if a tablet is not available).

   Those deemed eligible after completing the screener will be asked for their contact information, and will be contacted over the phone or email shortly after initial contact. University staff will offer information about the study over the phone and options for confirming their HIV negative status. If a participant wants to visit a partner CBO testing site or university site (Emory and Hunter), university staff will schedule an appointment for HIV testing. If a participant wants to take an at-home HIV test, university staff will mail out a FDA approved at-home HIV test.

   After taking an at-home HIV test or testing at a partner CBO testing site or university site (Emory and Hunter), participants will follow the same procedure as described under "Recruitment through online, print, and telephone ads."

   For those who screen ineligible, the device will display ineligibility information and ask the participant if he would like to consent to enter his contact information for consideration in future studies. When paper and pencil are used, participants will provide their contact information if they are interested in participating in Keep It Up! or other studies; they will not be aware of their eligibility at the time. The tablet (and paper form) includes a question in the contact information section asking for consent to add participants to the IMPACT database. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected on the tablet through Assessment Center will be securely uploaded to the tracking system. Information collected with paper and pencil will be manually entered by research study staff into Assessment Center within 3 days of receipt.

3. **Recruitment through community partner referrals.** Participants recruited through referrals from community partners will be given a business card with a pre-generated screener code and a link to an online screener after testing HIV negative. The screener codes on these business cards will only be valid for three months from the date that they are given to community partners. New batches of business cards with valid screener codes will be regularly distributed

to partner sites. Once the screener code expires, the participant will no longer be able to use it as verification that they have recently tested HIV negative.

The participants will use the link to access a study webpage for detailed project information and a brief eligibility screener. Interested participants will provide contact information (name, phone, email address) and complete the screener, including the screener code as proof that they have recently tested negative at a community partner site. If eligible, they will be sent an automatic enrollment email with a link to the KIU! study.

For those who screen ineligible, the online screener will ask the participant if he would like to consent to enter his contact information for consideration in future studies. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected from the online screener will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff within 3 days of receipt.

4. **Recruitment through referrals from ongoing studies and research participant registries.** Participants who become interested in the study through referrals from ongoing studies or IRB approved research participant registries at the university sites will be directed to a study webpage for detailed project information and a brief eligibility screener. Interested participants will follow the same procedure as described under “Recruitment through online, print, and telephone ads.”

5. **Recruitment through CDPH clinics.** At the conclusion of an HIV testing appointment, the CDPH staff member will give male clients who have tested HIV negative, and appear to be between the ages of 18 and 29, a brief description of the study. They will mention to the client that CDPH is working with Northwestern University researchers on the Keep It Up! study as a way to learn more about the health behaviors and outcomes of young men who have sex with men (YMSM). The CDPH staff member will briefly mention features of the study, such as it being a paid, online HIV prevention research study. To minimize the risk for coercion, the CDPH staff member will emphasize the optional nature of participation and that it will not affect, in any way, their access to healthcare services. The CDPH staff member will ask the client if he is interested in hearing more details about the study and possibly screening to see if he is eligible. If the client indicates that he is interested, the CDPH staff member will walk the client over to a Keep It Up! staff member who is stationed in another private room at the clinic. CDPH staff contact with participants will be limited to the referral of participants to the study and will not include performing informed consent or enrolling participants into the study.

   The Keep It Up! staff member will give more details about the study (e.g. randomization, timeline, and study components). To minimize the risk for coercion, the staff member will reiterate the optional nature of participation and that it will not affect, in any way, their access to healthcare services at CDPH. If the client still appears interested, the Keep It Up! staff member will invite them to screen for the study.

   The client will complete the online screener using a computer or tablet (or paper form if necessary) in the private room. If eligible, an enrollment email with a link to the study to be sent to the participant’s email address. The Keep It Up! staff member will inform the participant of the opportunity to complete the baseline assessment and STI testing while on-site at the clinic. If a participant prefers to complete the baseline assessment and STI testing at home, before starting the baseline assessment he will complete an online consent form that outlines the at-home STI testing process. If a participant prefers to complete the baseline assessment and STI testing while on-site at the clinic, before starting the baseline assessment, he will complete a paper consent form that outlines the STI testing process during clinic visits.

Most clients who test for HIV at a CDPH clinic will also have already been tested for urethral and rectal STIs as a part of their clinic visit. STI test samples are shipped to University of Illinois at Chicago (UIC) lab for analysis. Participants who have already completed STI testing will be asked to consent to the clinic's UIC lab sharing their results with study staff via fax. KIU! staff will call the lab client services and provide the patient name, date of birth, and date of specimen collection in order to verify that correct results are sent. In addition, KIU! staff will verify the fax number to which the results should be sent. The fax machine to which results will be sent is located in the mail room of Northwestern's Department of Medical Social Sciences (MSS). The MMS office is not open to the general public. The office is only accessible to staff with ID cards and invited guests who are buzzed into the office. Guests are typically escorted through the office by staff. In general, only MSS staff access the fax machine. To protect participant's confidentiality, KIU! staff will ask the lab to confirm the time that the fax will be sent so that the results are immediately retrieved from the fax machine. All faxes of results will also include a fax cover sheet that describes the confidential nature of the contents and has instructions to notify the sender to report any faxes received in error and destroy the misdirected documents. The cover letter also warns that any mishandling of the documents, such as copying or dissemination, is illegal.. It typically takes 3 – 7 days for the return of results. CDPH staff will be responsible for providing these participants with treatment and reporting positive results to appropriate authorities. Upon completing the baseline assessment, the participant will be compensated $50 cash and will be emailed a link to the first session of the intervention.

Clients who have not completed STI testing as indicated by the study (i.e., urethral and rectal testing for chlamydia and gonorrhea) during their clinic visit or decline to consent to the clinic's UIC lab sharing their test results will have the option to take the test kits home, be mailed the test kits by university staff, or self-administer the test kits while still on site at the CDPH clinic.

Clients who take the kits home or have the kits mailed to their home will also have to complete the baseline assessment at home. These clients will complete the online consent form before beginning the baseline assessment, self-administer the STI tests, and mail the completed kits to the CDC for analysis. Upon receipt of their test kits by the CDC, they will be compensated $30 in Visa gift cards and emailed a link to the first session of the intervention.

For participants who choose to self-administer the STI tests on-site at the CDPH clinic, the completed kits will be mailed by Keep It Up! staff to the CDC lab for analysis. Samples that are not mailed out the same day will be stored in a locked storage cabinet by university staff for no more than 7 days before being mailed to the CDC. Upon completing the baseline assessment and STI testing, the participant will be compensated $50 cash and will be emailed a link to the first session of the intervention.

Keep It Up! staff will be trained in appropriate and ethical methods of recruiting participants in medical settings. All Keep It Up! staff will complete Human Subjects Research CITI training before taking part in any recruitment, consenting, or enrollment activities. CDPH staff contact with participants will be limited to referring participants to the study and will not include performing tasks, such as collecting informed consent, for which Northwestern University requires Human Subjects CITI Training. CDPH staff will be trained by Keep It Up! staff through PowerPoint presentation and handouts on the background, rationale, and set up of the study. CDPH staff will also be given a verbal script with basic study information that they can use to refer participants to the study. The importance of emphasizing the optional nature of participation and that it will not affect, in any way, clients' access to healthcare services will be stressed during CDPH staff trainings. The CDPH supervising physician, who will also act as the study liaison, has also completed Human Subjects Research CITI training and will be able to offer ongoing guidance to CDPH staff on appropriate ways to refer clients to the study.

Eligible participants across all study sites will be offered the opportunity to visit Emory University, Hunter College, or Northwestern University to complete the baseline assessment and complete their first set of self-administered STI test kits.

**B.4. Consent/assent/parental permission procedures.**

The consent process will differ depending on the source from which a participant is recruited.

**CBO Recruitment.** At the conclusion of their post-test appointment or rapid-test, YMSM who test HIV negative will be given a tablet computer by the staff member who conducted the HIV test (with paper-and-pencil backup as necessary).We will apply the recruitment, consent, and enrollment procedures used successfully in our developmental R34; however, we will streamline the process and utilize tablet PC devices, in addition to paper and pencil, to recruit and screen participants. The tablets (or paper form) will display information about the study, ask the potential participant demographic questions, and whether or not he wants to be contacted by study staff. If so, the device will ask for contact information. If not, the tablet will ask questions assessing reasons for nonparticipation. When paper and pencil are used, participants will provide their contact information if they are interested in participating in Keep It Up! or other studies; they will not be aware of their eligibility at the time. An alteration of consent and waiver of documentation will be requested from the IRBs for this screener. Information collected on the tablet will be encrypted on the device and securely transmitted to the Assessment Center server by staff. (The AC platform was designed for measuring patient reported outcomes in health research and care, and is built upon a technologically rich, reusable software platform that can be accessed, managed, and shared by researchers.) Device log-ins will prevent unauthorized access to the encrypted information on the device. Information collected on the tablet using the iFormBuilder app will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff. The CSV files will be password protected. Information collected with paper and pencil will be manually entered by research study staff into Assessment Center within 3 days of receipt. Paper forms will be stored in locked cabinets or other similar storage units.

YMSM interested in participating will be instructed to expect an e-mail with more information about the study and told that they can use Internet-enabled computers at their local recruitment site for free. The research coordinators based in Chicago, Atlanta, and New York will be on hand to provide training and support to testing staff to assure easy compliance with this recruitment procedure. Potential participants will be sent a recruitment e-mail to the address entered into the tablet (or written on paper form); we will solicit email addresses that are checked regularly. The participant will be given the option to immediately be considered for participation, defer participation to a specified later date within 4 weeks (e.g. a vacation preclude immediate enrollment), or have their information removed from the contact database. Non-response to the recruitment e-mail after 4 days will trigger the retention protocol that will include further e-mails, phone calls if a valid phone number was provided, a text message (if consent provided). Individuals who wish to be considered for participation will complete a brief online questionnaire that will assess inclusion criteria, and if eligible will be enrolled and directed to the baseline survey.

The only data collected prior to informed consent will be screening data used to assure eligibility and reasons for non-participation. Consent will be conducted online using procedures that have previously been IRB approved and used successfully in our developmental R34. The consent document will be written to Federal OHRP standards with 8$^{th}$ grade or below reading level. The consent statements will have the required elements of informed consent, including: (1) a description of the study and the amount of time required for participation; (2) acknowledgment that participation is voluntary and that no negative consequences will occur for those who choose not to participate; (3) acknowledgment of the participant's right to withdraw at any time; (4) guarantee of confidentiality unless any person is in danger of injury; (5) a statement of payment, including amount and circumstances under which the respondent would not be paid (including early withdrawal from the study); and (6) contact information for relevant investigators and IRB members. The consent form will also specify that positive STI test results will be reported to the Department of Public Health in accordance to their reporting procedures.

**Recruitment through online, print, and telephone ads.** Participants recruited through these ads will be directed to a study webpage for detailed project information and a brief eligibility screener. The participant is then asked if he is willing to complete the brief Eligibility Screener to determine if he is eligible to participate.

If he consents by clicking yes, his consent will be saved in a CSV file and later manually entered and saved into Assessment Center database as a data point. Once consent is given, the online Eligibility Screener form asks questions about demographics, including age, sex, sexual orientation, relationship status, and sexual behaviors. If the participant appears to be eligible, he will be asked to provide contact information so that study staff can follow-up and help him schedule an HIV test at a testing site or mail him an at-home HIV test kit to confirm his HIV negative status.

Participants who choose to receive an at-home HIV test kit will be emailed a link to an online consent addendum hosted on the secure REDCap website. Participants who choose to be mailed a Home Access at-home specimen collection kit will be asked to consent to allowing Home Access to share their results with university staff. HIV results will be shared between Home Access and Northwestern University via SFTP. Participants who choose to be mailed an Oraquick at-home HIV test will be asked to consent to uploading a photo of their test stick to a secure website or calling university staff to report their results. Participants' consent to these procedures will be saved as a data point in REDCap and trigger study staff to mail out the at-home HIV test kit. University staff will use this information to confirm participants' eligibility for the study. If a participant does not consent to share his results with university staff, he will be told that he is unable to participate in the study without confirming his HIV status with university staff.

***For participants who visit testing site.***
After the participant takes an HIV test and confirms his HIV negative status, the testing counselor will provide the participant with a tablet (or paper form) to complete the full screener and confirm eligibility. If eligible, an email with a study link to be sent to the participant. After clicking this link, the participant will provide online consent before beginning the study. Participants read through our online consent form and click either "I Agree" or "Decline". Their responses are collected and stored in the Assessment Center database.

If the participant is ineligible, the online screener (or paper form) will ask if the participant would like to be contacted for other studies. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. When consent is collected it will be saved in a CSV file and later manually entered and saved into the Assessment Center database.

***For participants who take at-home test (Home Access)***

After the participant collects his blood specimen, he will mail it back to Home Access for analysis. The participant must use the pre-paid and pre-addressed envelope provided by Home Access to return their blood sample. After shipping his blood specimen, the participant will call a toll-free number after seven days to receive his test results and post-test counseling. Home Access will also share the results with Northwestern University via SFTP. If the participant tests negative, the project coordinator will call the participant to do a full screening over the phone and confirm eligibility. If eligible, an enrollment email with a link to the study to be sent to the participant's email address. After clicking this link, the participant will provide online consent before beginning the study. Participants read through our online consent form and click either "I Agree" or "Decline". Their responses are collected and stored in the Assessment Center database.

If ineligible, the project coordinator will let the participant know that he is ineligible for KIU! but may be eligible for other studies. If the participant is interested in other studies, the project coordinator will collect additional contact info and enter it into the IMPACT database. All subjects will have to consent to being added to the IMPACT database.

***For participants who take at-home test (OraQuick)***

After the participant takes an at-home HIV test, he will be required to interpret his test result by comparing his test stick to the pictures and descriptions on test kit directions. After determining his test result, the participant will need to upload a photo of his test stick or call study staff to report his test result. If the test result is negative, the project coordinator will do a full screening with the participant over the phone and confirm eligibility. If eligible, an enrollment email with a link to the study to be sent to the participant's email address. After clicking this link, the participant will provide online consent before beginning the study. Participants read through our online consent form and click either "I Agree" or "Decline". Their responses are collected and stored in the Assessment Center database.

If ineligible, the project coordinator will let the participant know that he is ineligible for KIU! but may be eligible for other studies. If the participant is interested in other studies, the project coordinator will collect additional contact info and to enter it into the IMPACT database. All subjects will have to consent to being added to the IMPACT database.

**Recruitment through street outreach.** University staff and interns will approach potential participants in various venues that cater to YMSM (e.g. bars, clubs, bathhouses, and festivals) and request the participant's permission to tell him about the study. If the participant consents, university staff and interns will explain the purposes of the study and invite him to answer questions that screen for preliminary eligibility. If the participant is interested, he will answer questions privately on a tablet (or paper form if a tablet is not available).

Those deemed eligible after completing the screener will be asked for their contact information, and will be contacted over the phone or email shortly after initial contact. University staff will offer information about the study and options for confirming their HIV negative status. If a participant wants to visit a partner CBO testing site or university site (Emory and Hunter), university staff will schedule an appointment for HIV testing. If a participant wants to take an at-home HIV test, university staff will mail out a FDA approved at-home HIV test. After taking an at-home HIV test or testing at a partner CBO testing site or university site (Emory and Hunter), participants will follow the same consent procedure as described under "Recruitment through online, print, and telephone ads."

For those who screen ineligible, the tablet will display ineligibility information and ask the participant if he would like to consent to enter his contact information for consideration in future studies. When paper and pencil are used, participants will provide their contact information if they are interested in participating in Keep It Up! or other studies; they will not be aware of their eligibility at the time. The tablet (and paper form) includes a question in the contact information section asking for consent to add participants to the IMPACT database. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected on the tablet through Assessment Center will be securely uploaded to the tracking system. Information collected with paper and pencil will be manually entered by research study staff into Assessment Center within 3 days of receipt.

**Recruitment through community partner referrals.** Participants recruited through referrals from community partners that do not perform direct, full recruitment for KIU! will be given a business card with a pre-generated screener code and a link an online screener after testing HIV negative. The screener codes on these business cards will only be valid for three months from the date that they are given to community partners. New batches of business cards with valid screener codes will be regularly distributed to partner sites. Once the screener code expires, the participant will no longer be able to use it as verification that they have recently tested HIV negative.

The participants will use the link to access a study webpage for detailed project information and a brief eligibility screener. The participant is then asked if he is willing to complete the brief Eligibility Screener to determine if he is eligible to participate.

If he consents by clicking yes, his consent will be saved in a CSV file and later manually entered and saved into Assessment Center database as a data point. Once consent is given, the online Eligibility Screener form asks questions about demographics, including age, sex, sexual orientation, relationship status, and sexual

behaviors. The participant will also be prompted to enter the screener code from the KIU! business card to verify that he has recently tested HIV negative. If the participant appears to be eligible, an automatic email with a study link will be triggered to be sent to the participant. After clicking this link, the participant will provide online consent before beginning the study. Participants read through our online consent form and click either "I Agree" or "Decline". Their responses are collected and stored in the Assessment Center database.

For those who screen ineligible, the online screener will ask the participant if he would like to consent to enter his contact information for consideration in future studies. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. Information collected from the online screener will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff within 3 days of receipt.

**Recruitment through referrals from ongoing studies and research participant registries.** Participants who become interested in the study through referrals from ongoing studies or IRB approved research participant registries at the university sites will be directed to a study webpage for detailed project information and a brief eligibility screener. Interested participants will follow the same consent procedure as described under “Recruitment through online, print, and telephone ads.”

**Recruitment through CDPH clinics.** At the conclusion of an HIV testing appointment, the CDPH staff member will give male clients who have tested HIV negative, and appear to be between the ages of 18 and 29, a brief description of the study. They will mention to the client that CDPH is working with Northwestern University researchers on the Keep It Up! study as a way to learn more about the health behaviors and outcomes of young men who have sex with men (YMSM). The CDPH staff member will briefly mention features of the study, such as it being a paid, online HIV prevention research study. To minimize the risk for coercion, the CDPH staff member will emphasize the optional nature of participation and that it will not affect, in any way, their access to healthcare services. The CDPH staff member will ask the client if he is interested in hearing more details about the study and possibly screening to see if he is eligible. If the client indicates that he is interested, the CDPH staff member will walk the client over to a Keep It Up! staff member who is stationed in another private room at the clinic. CDPH staff contact with participants will be limited to the referral of participants to the study and will not include performing informed consent or enrolling participants into the study.

Prior to administering the eligibility screener, university staff will request the client’s permission to tell him more about the study using a computer or tablet (or using pencil and paper, as necessary). The Keep It Up! staff member will give more details about the study (e.g. randomization, timeline, and study components). To minimize the risk for coercion, the staff member will reiterate the optional nature of participation and that it will not affect, in any way, their access to healthcare services at CDPH. If the client still appears interested, the Keep It Up! staff member will invite them to screen for the study. If the client consents to this, he will be given detailed information about the study on the computer or tablet (or paper form). The participant is then asked if he is willing to complete the brief online eligibility screener to determine if he is eligible to participate.

If he consents by clicking yes (or checking yes on the paper form), this consent will be documented as a data point in the Assessment Center database (if paper form used is used, the participant’s consent will be manually entered and saved into Assessment Center database as a data point). Once consent is given, the online eligibility screener form (or paper form) asks questions about demographics, including age, sex, sexual orientation, relationship status, and sexual behaviors.

If the participant is eligible, he will be asked to provide contact information so that study staff can email him the study link and to maintain contact throughout the course of the study. The university staff member will inform the participant of the opportunity to complete the baseline assessment and STI testing while on-site at the clinic. If the participant agrees, the university staff member will present him with a paper consent form that gives more information about the STI testing process on site. Participants who completed STI testing during

their clinic visit will also be asked to consent to the clinic's UIC lab sharing their STI results with study staff. After consenting to the on-site baseline and STI testing process, the participant will access the study using the link that we send via email. If the participant prefers to complete the baseline assessment and STI testing at home, before beginning the baseline assessment, he will be given an online consent form that outlines the at-home STI testing process.

If the participant is ineligible or not interested in taking part in Keep It Up, the computer (or paper form) asks if the participant is interested in other studies. If the participant would like to be contacted for other studies, the tablet (or paper form) prompts the participant to give his contact information. All subjects will have to consent to being added to the IMPACT database before research staff approaches them about participating in other studies. When consent is collected on the tablet, it will be captured and documented in Assessment Center. When consent is collected on paper, it will be manually entered and saved into the Assessment Center database.

**Participants who complete the baseline assessment and STI testing on-site at Emory University, Hunter College, or Northwestern University.** Across all study sites, participants who have screened eligible will be offered the opportunity to visit Emory University, Hunter College, or Northwestern University to complete the baseline assessment and complete their first set of self-administered STI test kits. Upon arrival at the university site, participants will be given a paper consent form by KIU! study staff that gives more information about the STI testing process on site.

**Participants who complete an exit interview or a repeat STI interview.** Prior to administering phone exit interviews or repeat STI interviews, study staff will give participants a brief description of what the interview entails (e.g. reasons for interview, time commitment, and incentive). After providing this information, the study team will ask the participant to give verbal confirmation that they would like to take part in the interview and agree to be recorded. If the participant is not interested in taking part in the interview or being recorded, study staff will thank them for their time and end the phone call.

**Participants who complete the <u>Timed Post-Release Testing</u>.** After potential participants screen as eligible, study staff who contact them to describe KIU! in greater detail. If they are still interested in participating in the timed post-release testing, a research assistant will email potential participants a link to an online consent form. Once the participant has consented, a research assistant will email them a unique link to the first intervention session. If a potential participant is not interested in completing the post-release testing, study staff will thank them for their time and end communication.

**C. Data Management and Analysis**

**C.1. Data acquisition and transmission.**

**C.1.a. Psychosocial measures.** Similar procedures successfully used in the developmental study will be employed and assessments will be completed via the Internet using a Computer-Assisted Self Interview (CASI). To protect the integrity of the participant's data, the system will assign each individual a unique random ID number at study enrollment. This number will be used for all study data. Data on participation and completion of the assessments and modules will be separated from the participants' actual assessment data, to allow for participant tracking without access to their self-report data. We will store all data in databases that will be maintained on a password-protected and fire-walled servers, maintained by Assessment Center. Access to the system interface will require a separate password. Only the PI and the study coordinators will have access to this subdirectory. The PI will review all requests, current and future, to use the data. Any data files that are provided to other individuals will be stripped of identifiers other than random ID numbers.

The database linking participant identifying information to their subject number will be destroyed one year after the end of data collection, thus removing any link between subjects and data. We propose to keep the link between subject ID and identifying information for one year for two reasons. First, we want to assure that no one participates in the study more than once, so we want to make sure we check new participants against our existing roster. Second, we may be requesting funding to continue this study. If this happens, we will need to contact past participants to recruit them into the study. If funding is awarded, then participants

would be consented into a new protocol, which would inform them about the link to past data. If the study does not continue, then we will destroy the link.

All personnel will complete extensive training before they are granted access to identifying information. They will complete Human Subjects training at Northwestern University or other performance sites, which complies with federal guidelines delineated in 45 CFR Part 46. Personnel sign confidentiality statements that specify that if the participant's confidentiality is breached unintentionally, personnel will follow the procedures for reporting this breach to the Principal Investigator. The confidentiality statement also states that unintentional or deliberate violations of participant's confidentiality may result in termination depending upon the severity of the event. Personnel will also participate in training regarding data safety, confidentiality of participants, limits of confidentiality, and proper administration of the study protocol.

**C.1.b. STI testing.** Our approach to the distance STI testing follows Co-I Sullivan's effective protocol for the Checking In Study (see A.3.)

**C2. Data entry methods.**
Our data management procedures are similar to those currently in use in our other studies, however, we will streamline the process and utilize tablet PC devices, in addition to paper and pencil, to recruit and screen participants. Information collected on the tablet using the iFormBuilder app will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff. When paper and pencil are used during recruitment and screening, study staff will manually enter the information into the Assessment Center database. Contact information for participant tracking and follow-up visits will be entered by RAs in a password protected ACCESS database. All self-report measures will be administered via CASI. Data will be downloaded daily and merged into a central database coordinated by the Project Manager. All files will be password-protected, and any paper files will be stored in locked cabinets with access for authorized project staff only.

**C3. Data analysis plan.**
This is a two-group, active-control, RCT of an online intervention. The study's hypothesis concerns between-group differences in the change in HIV/STI risk behavior and STI incidence from pre-intervention to later follow-ups. There are 4 assessment points of RCT outcomes: baseline, 3, 6, and 12 months post-intervention. Prior to conducting full analyses, standard descriptive analyses will be conducted to check for invalid values, outliers, and logical consistency between variables. We will assess the comparability of the experimental and control groups at baseline. If any variables differ significantly at baseline, they will be included as covariates in the adjusted outcome analyses along with variables known from prior research (e.g. age) to be correlated with the outcome under analysis. Following extensive data description and analysis at separate follow-up points, the primary analysis will utilize all follow-up points by fitting mixed effect regression models. Also known as hierarchical linear models (HLM) [205-207], these models allow for the presence of missing data, time-varying or invariant covariates, and subject measurement at different time points. HLM models appropriate to the characteristics of the distribution (i.e. normal, Poisson) will be fit using SAS.

The primary behavioral outcome measure of treatment success will be the count of unprotected anal sex acts and the biomedical endpoint will be NG/CT incidence (Aim 2). Secondary outcomes include: condom errors, IMB factors, and receipt of an HIV test. We will also explore intervention effects separately for receptive and insertive anal sex. The primary independent variable of interest is the indicator for the intervention group. The baseline value of the outcome and other required covariates at baseline will be included as additional independent variables. The intervention will recruit participants from a variety of sources. Participants will be recruited (1) from the testing clinics and mobile testing units of our partner CBOs in Chicago, New York, and Atlanta, (2) using print, online, and recorded ads, (3) by referral from ongoing studies and IRB-approved research participant registries at the university sites, and (4) by referral from community partners who provide HIV testing. Regardless of recruitment source, prior to beginning the intervention, participants will still have the contact with an HIV testing counselor or study team member that is important for recruitment and retention. However it is not delivered in groups so site will be adjusted for as a fixed rather than a random independent

variable. A random intercept term will be included to account for individual average levels of the outcome. The effect of time will first be estimated as a categorical variable in order to describe and adjust for time trends as observed. A second strategy will start with estimating a single slope reflecting average change across all 4 time points, then add a quadratic term if it contributes significantly to the model. Random effects for time variables, reflecting individual variations in time trends, will be included in addition to random intercepts, if significant. A single effect of group will test the intervention effect averaged across all time points, adjusting for all included covariates and underlying time trends. Potential moderators (race/ethnicity, relationships status, and gay/bisexual identity) will be added as independent variables and their interactions with intervention group will be tested (Aim 3). Addition of interaction terms between time and intervention group will provide a test for comparing time trends in change scores between groups.

Analysis of all available measurements among all participants regardless of dose is consistent with an "intent-to-treat" perspective[172]. It is desirable to also perform an analysis which considers the "dose" and engagement in the intervention. We will use Rubin's causal modeling to consider dose-effect when making comparisons across the two groups[208,209]. Further, in our HLM models, missing data is assumed to be missing at random conditional on the independent variables in the model; therefore we are in effect assuming that participants with incomplete measurements would have been similar to others in their group (their same covariate values) with complete measurements.

**D. Quality Assurance**

**D.1. Procedures in place to ensure the validity and integrity of the data.**

All project staff (from investigators to research associates) have extensive experience interacting with our research populations in a sensitive and understanding manner so as to increase the comfort of research participants and ensure comprehensive and valid data collection. In addition, all have completed the required on-line training for the protection of human subjects. Our use of self-administered electronic systems for collecting data will also serve to enhance the reliability and validity of the data from each participant. Private self-report increases the proportion of individuals admitting sexual behaviors and illicit drug use. As such, these measurement modalities allow for greater respondent privacy and remove barriers to honest responding, such as embarrassment, feedback from interviewer facial expressions, and other social influences.

**D.2. Procedures in place to ensure the accuracy and completeness of the data.**

**D.2.a. Health Information Technology protocols.** Given the online nature of this study, our HIT team will include professional quality assurance staff who will provide software testing and troubleshooting for new and existing HIT systems, including development of test plans, test cases and test scripts. The HIT team will ensure that the intervention functionality operates properly and that the content is accurate, complete and clear.

**D.2.b. Data management protocols.** Our quality assurance plan also involves thorough management of study data. On a weekly basis, the Project Coordinator will download data from the Assessment Center. Based on our previous quality assurance practices with KIU! data, a line of data (24 columns) is generated for each question that a participant answers. Columns to be used for quality assurance are the participant's login pin ("PIN"), the instrument name ("Inst"), the item name ("Item ID"), the item order ("ItmOrder"), the participant's response ("score"), data type ("DataType"), and the date and time that a participant starts an instrument ("InstStr") and ends an instrument ("InstEnd"). (Instruments can be either measures or intervention modules). By using the start and end times listed for each item (formatted as 12/34/56 for date, and 12:34 for time), researchers can determine the length of time it takes to a participant to complete an instrument or a module. The "score" and "DataType" columns can be used to check the accuracy of participant responses. Participant's responses to questions are shown in the "score" column. The data type can be string (for responses typed into text boxes), integer (for responses to multiple choice questions), or bitwise (for responses chosen from a checkbox list). If the score output does not match up correctly with the format expected for the data type, we can take steps to correct the data collection. In addition, we can determine if the data collection program has incorrectly skipped questions by looking at the list of item names and item order as well as if questions have been skipped by participants ("SKIP" will appear in the score column).

**E. Regulatory Issues**
**E1. Reporting of SAEs.**
**E1a. Medication trials: to the IRB, NIDA, and, as applicable to the FDA.** Not applicable.
**E1b. Non-medication trials: to the IRB and NIDA.** See F2 below for details.

**E2. Reporting of IRB actions to NIDA.**
All communication from the NU IRB, in response to any reports filed, will be immediately conveyed to NIDA upon receipt from the IRB. See F2 below for additional details.

**E3. Report of changes or amendments to the protocol.**
Any changes or amendments to the study protocols will be approved by the NU IRB and by NIDA prior to their implementation in the study.

**E4. Trial stoppage rules.**
The NU IRB has the authority to suspend or terminate approval of any research at its site that has been associated with unexpected serious harm to participants. The conditions under which the study would be stopped include, but are not limited to, a direct causal link between the study conditions and the hospitalization, impairment, or death of any research participants.

**E5. Disclosure of any conflict of interest in the DSM.**
No conflict of interest in the DSM exists for any key personnel on the study.

**F. Trial Safety**
**F.1. Potential risks and benefits.**
**F.1.a. Potential risks** consist of the actual assessment and recruitment process (e.g., potential coercion, discomfort or distress during the intervention or assessments), breaches of confidentiality, and HIV seroconversion or STI diagnosis during the course of the study. It is possible that certain assessment items (e.g. sexual or drug behavior; STI and HIV testing results) may make participants feel uncomfortable. There is a small possibility that a participant's information could be intercepted while in transit over the Internet or that data could be hacked from our servers. It is also possible that participants will experience a loss of confidentiality if they complete the assessments or intervention modules in a public space. Finally, a participant could test positive during the course of the study, however we have established procedures set up at each clinic linking participants to services and care.

**F.1.b. Exit Interview and repeat STI interview Risks.** It is possible that certain questions asked during the interview (e.g., questions about the acceptability of rectal STI testing) may make participants feel uncomfortable. Participants will be reminded that they can refuse to answer any questions that they are uncomfortable answering. There is a small possibility that a participant's interview audio and transcription could be hacked from our servers where the files will be saved. It is also possible that participants will experience a loss of confidentiality if they complete the exit interview in a public space. We have established procedures to protect against these potential risks (see Section C.2.a.8).

**F.1.c.Timed Post-Release Testing Risks.** It is possible that some of the content in the intervention modules and booster sessions may make participants feel uncomfortable. Participants will be reminded that they can call a research staff member about anything that can come up during the study. We will also refer participants to counseling services if they want. They will be reminded that they can stop participating at any time. It is also possible that participants my find some questions unpleasant or hard to answer. Participants will be reminded that they can stop the exit interview at any time and withdraw from the completing the timed post-release testing.

**F.1.d. At-Home HIV Testing Risks**. The risks of participating in at-home HIV testing include those associated with loss of confidentiality, fingersticks to draw blood, and returning test results. For participants who complete at-home testing using Home Access specimen collection kits, fingersticks may cause temporary discomfort and

rarely, infection. Some persons may pass out at the sight of blood, but this is rare. Disclosure of a preliminary positive result from a rapid HIV test or confirmed reactive HIV test result may cause distress and even substantial psychological trauma. Participants will be offered the number of a suicide prevention or other crisis counseling hotline in case of distress about preliminary positive or confirmed positive HIV test results.

Individuals who agree to participate in at-home HIV testing will receive post-test counseling and, if appropriate, be linked to care. The project coordinator will use established organizational linkage-to-care procedures that have been used in other IRB approved studies. Linkage-to-care will include referring the participant to a clinic that will conduct a free confirmatory HIV test, and to someone that will work with them receive treatment if their confirmatory test returns positive. In Atlanta, participants under 24 years old will be referred to the Ponce de Leon center at Grady while those who are 24 years and older will be referred to their county health department. In Chicago, participants will be referred to a linkage-to-care specialist at Center on Halsted. In New York, participants may be referred to the Mount Sinai Comprehensive Health Program, Callen-Lorde Community Health Center, or Gay Men's Health Crisis Prevention Center. For participants who live outside of Atlanta, Chicago, and New York, study staff will use the AIDS.gov service locator to make referrals to the nearest health care provider.

**F.1.e. There are several potential benefits** to this study. YMSM may benefit by reducing their risky sexual behavior, accessing HIV testing services, and decreasing their risk of HIV/STI infection as a result of program participation. Collaborating CBOs may benefit from the collected evaluation data by improving existing HIV testing services and delivering prevention programs to YMSM. Society will benefit from the creation of an intervention that reduces risk behavior among YMSM, limiting the spread of HIV/AIDS, and addressing health disparities. Possible risks are outweighed by the potential to reduce HIV/STI-risk among YMSM.

In addition to these general study benefits, the exit interviews and repeat STI interviews may provide information that can be used to refine future iterations of the intervention and better inform research efforts towards comprehensive at-home STI testing. As with the current intervention, these future iterations may benefit society by reducing risk behaviors among YMSM and limiting the spread of HIV and STIs.

**F.2. Collection and reporting of adverse events (AEs) and serious adverse events (SAEs).**
Our guidelines or the review and reporting of unanticipated problems and adverse events is taken from HHS regulations under 45 CFR part 46. Consistent with these guidelines, we recognize that only a small subset of adverse events occurring in human subjects participating in research are classified as unanticipated problems which must be reported under 45 CFR part 46. In the event that specific issues arise in the conduct of our research, our procedures will be guided by the following definitions and action steps (except where otherwise noted, all quoted language has been taken *from US HHS Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events* (http://www.hhs.gov/ohrp/policy/advevntguid.html):

1) An Adverse Event (AE) is defined as "any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research," AEs may include both physical and psychological harms.
2) A serious adverse event (SAE) is defined as "any untoward medical occurrence that results in death, is life-threatening, requires or prolongs hospitalization, causes persistent or significant disability/incapacity, results in congenital anomalies/birth defects, or in the opinion of the investigators represents other significant hazards or potentially serious harm to research subjects or others" (NIH OHSP).
3) Any event deemed to be an AE or SAE by the Principal Investigator, Dr. Brian Mustanski, will be documented in the study file. This documentation will include: a) a detailed description of the AE or SAE; b) details, data, and other supporting documentation regarding the extent to which the AE or SAE was related to participation in the research and specifying the participant's study arm; c) details, data, and other supporting documentation regarding the extent to which the AE or SAE was unexpected (i.e., representing a deviation or departure from study

protocols; d) a detailed description of follow-up that was immediately undertaken with the study participant, and outcome, if applicable; and e) a detailed description of any action plan proposed in response to the AE or SAE (to be reviewed and approved by the DSMB).

4) AEs will be reported to the NIDA at least once per year as a part of the annual progress report. The PI will describe each event, when it occurred, the study arm of the participant, and the outcome/resolution. If there were no AEs, a statement that no AEs occurred will be included in the progress report or otherwise communicated to the PO.
5) SAEs will be reported to the NIDA PO by email within 24 hours of the event of the investigator becoming aware of the event and the written follow-up will be submitted within 72 hours of the event. For any SAE, the Principal Investigator will then prepare a detailed report, regardless of whether the SAE is deemed related to research. This report will include all elements required by NIH and will also include completion of the NU Unanticipated Problem Report Form (see attached). This report will be submitted to: a) the NU IRB; b) the DSMB; and c) NIDA.
6) For AEs that are not SAEs, the Principal Investigator will then make a determination regarding whether the AE qualifies as an unanticipated problem. Consistent with OHRP guidance, we will consider an unanticipated problem to include any incident, experience or outcome that meets all of the following criteria:
    a. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
    b. related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
    c. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
7) Any AE that is also deemed to be an unanticipated problem will immediately be documented and reported to: a) the DSMB; b) the NU IRB; and c) NIDA (as per 45 CFR 46.103(b)(5)). As per OHRP recommendations for "prompt" reporting, all AEs deemed to be unanticipated problems will be reported to the IRB within 1 week of the investigator becoming aware of the event. This report will include:
    a. appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
    b. a detailed description of the adverse event, incident, experience, or outcome;
    c. an explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem; and
    d. a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.
8) Any AE that is not deemed to be an unanticipated problem will be reported to the DSMB and will be logged into study records. As per OHRP recommendations for "prompt" reporting, all AEs not deemed to be unanticipated problems will be reported to the DSMB within 1 week of the investigator becoming aware of the event. This report will include:
    a. appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
    b. a detailed description of the adverse event, incident, experience, or outcome;
    c. an explanation of the basis for determining that the adverse event, incident, experience, or outcome does not represent an unanticipated problem; and
    d. a description of any follow-up actions that have been taken or are proposed in response to the AE.
9) If the DSMB agrees with the Principal Investigator's determination that the AE is not an unanticipated problem, follow-up actions will be agreed upon between the DSMB and PI and will be documented accordingly. If the DSMB makes a determination that the AE is, in fact, an unanticipated problem, procedures will be followed as per #7, above.

10) In the event that an AE or SAE occurs, the PI will schedule a case discussion meeting within one month of the event. All relevant staff will attend this meeting. The PI will document the content of the case discussion, as well as the implementation of any additional trainings that emerged as part of an action plan following the meeting.
11) The PI, Dr. Mustanski, will be responsible for responding to and addressing all recommendations that result from monitoring activities.
12) The PI will notify NIDA of any actions taken by the IRB during continuing study review and of any major changes in the status of the ongoing protocol which would only occur with IRB approval. Such changes would include, but are not limited to: (1) amendments to the protocol; (2) temporary suspension of patient accrual, or of the protocol; (3) changes in informed consent or IRB approval status; (4) termination of participant accrual or of the protocol; or (5) other problems or issues that could affect the human subjects in the study.

**F.3. Management of AEs, SAEs, and other study risks.**

**F.3.a. Protection against AEs and SAEs.** All study personnel, particularly the study coordinators, will be trained regarding how to handle adverse events. Possible adverse events that are unanticipated will be brought to the attention of the Principal Investigator and reported immediately to the Northwestern University and other engaged institutions' IRBs. Given the online nature of the study, special procedures are required to identify adverse events. To identify adverse events we will instruct participants to report any adverse events to the research team as soon as possible via e-mail or phone; such a report will immediately be brought to the attention of the PI. Also, at each assessment, we will ask participants if they have experienced any adverse events. Their responses to these items will be programmed to be e-mailed to the research team upon submission, who will then immediately forward them to the PI.

The IRBs will determine whether it is appropriate to stop the study protocol temporarily or will provide suggestions and/or /modifications to the study procedures as necessary. Possible modifications include adding these possible adverse events to the consent form and re-consenting all study participants. The PI will be responsible for monitoring participant safety on a monthly basis at regularly scheduled research meetings. He will keep a written log of all events and ensure that the IRB is contacted immediately. He will also keep a log of the outcome of IRB decisions regarding adverse events and apprise the research team of any changes that need to occur as a result of IRB decisions.

**F.3.b. Protection in the recruitment and informed consent process**. We will apply the following recruitment procedures used successfully in our developmental R34; however, we will streamline the process and utilize tablet PC devices, in addition to paper and pencil, to recruit and screen participants. Clients can also be screened online on the Assessment Center platform or offline on the iFormBuilder app. The tablets (or paper form) will display information about the study, ask the potential participant demographic questions, and whether or not he wants to be contacted by study staff. If so, the device will ask for contact information. If not, the tablet will ask questions assessing reasons for nonparticipation. When paper and pencil are used, participants will provide their contact information if they are interested in participating in Keep It Up! or other studies; they will not be aware of their eligibility at the time. An alteration of consent and waiver of documentation will be requested from the IRBs for this screener. Information collected on the tablet will be encrypted on the device and securely transmitted to the Assessment Center server by staff. Device log-ins will prevent unauthorized access to the encrypted information on the device. Information collected on the tablet using the iFormBuilder app will be exported to a CSV file and either the information will be uploaded to Assessment Center or manually entered by research study staff. Information collected with paper and pencil will be manually entered by research study staff into Assessment Center within 3 days of receipt. Participants recruited through ads and referrals will complete an online screener using Limesurvey. The LimeSurvey software is hosted on the kiu2.org domain on a virtual private server with an SSL encryption certificate. Participants who choose to receive an at-home HIV test kit will be emailed a link to an online consent addendum hosted on the secure REDCap website. Participants' consent will be saved as a data point in REDCap and trigger study staff to mail out the at-home HIV test kit.

YMSM interested in participating will be instructed to expect an e-mail with more information about the study and told that they can use Internet-enabled computers at their local recruitment site for free. The research coordinators based in Chicago, Atlanta, and New York will be on hand to provide training and support to testing staff to assure easy compliance with this recruitment procedure. Potential participants will be sent a recruitment e-mail to the address entered into the tablet (or paper form); we will solicit email addresses that are checked regularly. The participant will be given the option to immediately be considered for participation, defer participation to a specified later date within 4 weeks (e.g. a vacation preclude immediate enrollment), or have their information removed from the contact database. Non-response to the recruitment e-mail after 4 days will trigger the retention protocol that will include further e-mails, phone calls if a valid phone number was provided, a text message (if consent provided). Individuals who wish to be considered for participation will complete a brief online questionnaire that will assess inclusion criteria, and if eligible will be enrolled and directed to the baseline survey.

Across all study sites, participants who have screened eligible will be offered the opportunity to visit Emory University, Hunter College, or Northwestern University to complete the baseline assessment and complete their first set of self-administered STI test kits. Upon arrival at the university site, participants will be given a paper consent form by KIU! study staff that gives more information about the STI testing process on site.

The only data collected prior to informed consent will be screening data used to assure eligibility and reasons for non-participation. Consent will be conducted online using procedures that have previously been IRB approved and used successfully in our developmental R34 (see Preliminary Studies). The consent document will be written to Federal OHRP standards with 8$^{th}$ grade or below reading level. The consent statements will have the required elements of informed consent, including (a) a description of the study and the amount of time required for participation; (b) acknowledgment that participation is voluntary and that no negative consequences will occur for those who choose not to participate; (c) acknowledgment of the participant's right to withdraw at any time; (d) guarantee of confidentiality unless any person is in danger of injury; (e) a statement of payment, including amount and circumstances under which the respondent would not be paid (including early withdrawal from the study); and (f) contact information for relevant investigators and IRB members.

Prior to administering phone exit interviews and repeat STI interviews, study staff will give participants a brief description of what the interview entails (e.g. reasons for interview, time commitment, and incentive). After providing this information, the study team will ask the participant to give verbal confirmation that they would like to take part in the interview and agree to be recorded. If the participant is not interested in taking part in the interview or being recorded, study staff will thank them for their time and end the phone call.

**F.3.c. Protection against potential coercion.** Any study that recruits participants from a healthcare setting has the potential for participants to feel coerced into participating. The investigators have extensive experience confronting the ethical issues of participant recruitment in clinical settings. We will work with all involved IRBs to assure compliance with ethical and HIPPA standards. Specifically, testing staff will not be given incentives for recruiting participants, and we will make it clear to participants that their decision regarding participation will not affect, in any way, their access to healthcare services.

**F.3.d. Protection against discomfort.** Multiple IRB-monitored studies at Northwestern University and our collaborating sites have used these or closely related measures with no known adverse effects. Participants will be told that they do not have to answer any question they do not wish to. Participants will be instructed that they can take a break and return to the online assessments or modules at a later time if they are experiencing mild distress. In the unlikely event that a participant experiences considerable distress they will be instructed to contact the Tracking Coordinator, who will refer them as appropriate to either the PI (who is a Licensed Clinical Psychologist) or the local project coordinators who can assist in making appropriate local referrals.

**F.3.e. Protection against a breach of confidentiality.** We will take several steps to prevent a breach of confidentiality.

***F.3.e.(i). Data handling, transmission, and storage.*** We have developed systematic protocols for data handling and storage over longitudinal online studies. Assessment Center (AC) has multiple mechanisms for providing data security in the transfer of data from client machines to AC servers. These webservers use Secure Socket Layer (SSL or https) technology to encrypt data exchanged between the client and the server. SSL will be implemented in all systems built for the project to ensure the encryption of data during transmission from the participants' workstations to AC servers. All project data will be stored on secured, password-protected database servers behind passcode-protected doors. All components of the data system will be accessible only through a login and password unique to each assigned user on the study team. The security access levels for these login accounts will be tiered based on specific roles and responsibilities for the project. The features and privileges associated with each role and subsequent access level will be determined based on the level of access to confidential data needed by each team member. For example, only project staff who maintain personal contact with participants will be given access to personal identifying information. Tracking staff will not be given access to survey data so they cannot link identifying information to participant data. All other team members will only have access to data that are tied to a random ID number that cannot be used to personally identify the participant. Database administrators in the Health Information Technology (HIT) group in the PI's Department at Northwestern who manage the AC technology will only access the database with names and contact information when absolutely necessary for maintaining the database.

The HIT technical staff will also work with study collaborators to develop standard protocols for maintaining a secure environment for data submission from the clinic to the AC servers, including potentially implementing a Virtual Private Network (VPN) connection that will be used to enter identifying information, to provide an additional layer of encryption for that sensitive data.

Participants recruited through ads and referrals will complete an online screener using Limesurvey. The LimeSurvey software is hosted on the kiu2.org domain on a virtual private server with an SSL encryption certificate. Only the PI and IMPACT Program webmaster have the passwords to the root folder of the virtual private server. All data collected by LimeSurvey will be saved as CSV files in password protected folders on a secure university shared drive.

Participants who complete at-home HIV testing using the Oraquick test kit will upload photos of their test kit to a data collection page on REDCap website. REDCap is hosted on Northwestern University's servers. Photos of the test sticks, linked to the participant's unique study ID, will be saved on a secure university shared drive for up to three months. This timeframe will allow participants up to three months from the date they tested HIV negative to fully enroll into the study.

***F.3.e.(ii). Separate databases.*** All names and contact information for the follow-up of participants will be stored in a database that is separate from the participant's responses to the screener and the assessment. Only a random study ID will be stored with the participant's data for linkage to subsequent data later. Staying consistent with information provided to participants in the consent form, data sources will be purged two years after the end of the study in 2017. De-identified data will be stored indefinitely on secure shared drives housed on Northwestern's servers.

***F.3.e.(iii). Staff training.*** All study staff, including HIT staff, will be trained in Human Subjects research and will sign confidentiality agreements prior to participation in the project.

***F.3.e.(iv). Certificate of Confidentiality.*** As we have done in over five prior studies, we will obtain a Certificate of Confidentiality. This Certificate helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. The Certificate of Confidentiality does not prevent disclosure under the following situations:

1) Physical or sexual abuse of a child by a parent or someone legally responsible for a child will be reported to the proper authorities.
2) Abuse of an elder person will be reported to the proper authorities.
3) Intent to harm one's self or someone else will be reported to the proper authorities.
4) If we need to protect the rights or welfare of research participants (for example, if they are hurt and need emergency care).

***F.3.e.(v). Participant assessments.*** To help protect participants' confidentiality while they complete the Internet-based assessments and intervention modules, we will: (1) remind participants each time they log on that they will be answering personal questions; (2) encourage them to complete the modules and questionnaires in a private environment; and (3) suggest spaces with greater privacy (e.g., in their dorm room with the door closed, at a coffee shop in an area where no one can look over their shoulder, etc.).

***F.3.e.(vi). Exit interviews and repeat STI interviews***. To help protect participants' confidentiality while they complete the exit interviews and repeat STI interviews, we will: (1) administer and record the interview in a private office space; (2) encourage participants to complete the interview in a private setting; (3) immediately transfer the recording of the interview from the digital recorder to a password protected folder on a secure university shared drive that only the study team can assess; (4) delete the interview from the digital recorder as soon as the audio file is uploaded to the secure university shared drive; and (5) save transcriptions of the audio recording to the secure university shared drive that only the study team can assess.

***F.3.e.(vii). Remote STI testing protocol.*** We have also developed procedures with the STI testing laboratory at the CDC to prevent a breach of confidentiality. (1) Participants will be given unique user IDs and passwords for all STI testing materials and for accessing STI test results. (2) Electronic communications with the CDC lab will be conducted via secure email. This includes de-identified STI test results to research study staff. (3) At the CDC lab, all STI test results will only be provided to the research team with evidence of an IRB-approved research protocol. (4) For participants who collect the urine and rectal samples on-site at Emory University, Hunter College, or Northwestern University, samples that are not mailed out the same day will be stored in a locked storage cabinet by KIU! study staff for no more than 7 days before being mailed to the CDC. The APTIMA Combo 2 Assay collection and transport tubes contain solution that protects the samples from degradation during storage. Urine samples can be stored for up to 30 days and rectal swabs can be stored for up to 60 days without refrigeration. Clinical specimens collected for this study will be tested for Chlamydia trachomatis and Neisseria gonorrhoeae. Clinical specimens collected for this study will be tested for Chlamydia trachomatis and Neisseria gonorrhoeae. Any remaining specimen material will be unlinked from patient identifiers and stored by the CDC, up to 20 years, for possible future bacterial or viral research. Any future studies with these specimens will not involve analysis of human nucleic acid.

Participants who are recruited from CDPH clinic sites and complete STI testing as a part of their clinic visit will be asked to authorize the clinic's UIC lab sharing their STI results with the study team. Participants will be asked to read and sign a consent form that includes a section on HIPAA Authorization to Use or Disclose Health Information that describes which personal health information will be shared and how this health information will be shared.

Participants who live abroad at the time of their 12 month STI test and complete testing outside of the U.S. will be asked to authorize their healthcare provider sharing their STI results with the study team. Participants will be asked to read and sign an authorization form that describes which personal health information will be shared and how this health information will be shared. Participants will be instructed to sign the authorization form, scan or take a high quality photo of the form, and email it back to the study team.

To help protect participants against a breach of confidentiality, all results from CDPH clinic sites or healthcare providers of participants living abroad will be shared via fax as the HIPAA Privacy Rule allows protected health information to be shared in this manner. KIU! staff will call the lab client services and provide the patient name, date of birth, and date of specimen collection in order to verify that correct results are sent. International

healthcare providers will be provided with this information on the authorization form that will be securely faxed to them by study staff. In addition, KIU! staff will verify the fax number to which the results should be sent. The fax machine to which results will be sent is located in the mail room of Northwestern's Department of Medical Social Sciences (MSS). The MMS office is not open to the general public. The office is only accessible to staff with ID cards and invited guests who are buzzed into the office. Guests are typically escorted through the office by staff. In general, only MSS staff access the fax machine. KIU! staff will ask the lab to confirm the time that the fax will be sent so that the results are immediately retrieved from the fax machine. All faxes of results will also include a fax cover sheet that describes the confidential nature of the contents and has instructions to notify the sender to report any faxes received in error and destroy the misdirected documents. The cover letter also warns that any mishandling of the documents, such as copying or dissemination, is illegal.

In order to avoid data entry errors and sharing incorrect results with participants, the study team will do comprehensive checks on logged results and the PDFs of results sent to participants. First, in order to get a list of new STI results to be entered into REDCap and shared with participants, one of the two research assistants will apply filters to the running spreadsheet of results received from the CDC. Second, the Project Director and other research assistant will double check that the list is accurate. Once the list is confirmed as accurate, a research assistant will log them in REDCap and prepare PDFs of results to send to participants. Finally, the Project Director will check the results logged in REDCap as well as the PDFs before they are sent to participants. For individual results received from CDPH, the Project Director will compare the lab report to the results logged in REDCap and the PDF draft of results. In addition to this system of checks, the study Data Manager will perform quality assurance every two weeks on all STI data entered in REDCap.

***F.3.e.(viii) At-home HIV testing protocol.*** We have also developed procedures with Home Access Health Corporation to prevent a breach of confidentiality: (1) Participants will be given a unique 11 digit code number for all specimen collection kit materials and for accessing HIV test results. (2) Electronic communications with Home Access will be conducted via SFTP. HIV test results linked to unique 11 digit code number will be shared with research study staff through the SFTP. (3) At Home Access, all HIV test results are stored on a secure, password-protected server and the results will only be provided to the research team with evidence of an IRB-approved research protocol. (4) Blood specimens collected for this study will be tested for HIV-1. Any remaining specimen material will stored by Home Access for up to 3 months before being disposed. The storage of blood samples for up to 3 months is part of the Home Access standard testing protocol approved by the FDA in 1996. The samples are not retested or used for any other purposes while stored.

Participants who complete at-home HIV testing using an Oraquick test kit will be given a unique five digit code for all HIV testing materials. We will ask that participants only share their results by uploading a photo of their test stick to a secure website or calling a university staff member. Participants who use Oraquick test kits will be responsible for disposing their oral swabs.

***F.3.e.(ix) Participant contact via email.*** The majority of our messages to participants are automatically sent to participants through Assessment Center and other survey programs to reduce change of human error. Most messages not automatically sent are individualized messages sent to one participant at a time. Our protocol also instructs study staff to never send group emails without using blind carbon copying (bcc). We will use mail merge software for emails that need to go to more than one participant rather than sending group emails. Mail merge only sends one email to each participant. No participants will be carbon copied on an email sent via mail merge. If, for any reason, it is ever preferable to send a group email using bcc, the email will be reviewed by at least two staff members before it is sent out.

***F.3.e.(x) Participant contact via text.*** When texting our participants, we will frequently use a service, Red Oxygen, that allows us to send texts from our secure Northwestern Outlook email accounts. Red Oxygen users can send messages to specific participants as well as bulk messages to lists of participants. Red Oxygen's Outlook add-on allows users to email individual text messages to participants and also receive and follow-up on responses through their Outlook account. Red Oxygen also offers standalone bulk texting software (Bulk

SMS) that gives users the ability to email large text message blasts through their Outlook account. When bulk messages are sent, each recipient will only see the designated Keep It Up! phone number tied to our Red Oxygen account. They will not see the phone numbers of other participants. As with the individual messages, all responses to bulk messages are routed to KIU! staff's Northwestern Outlook email account. Red Oxygen follows the National Privacy Principles as set out in the Privacy Act 1988 (Cth) and the Privacy Amendment (Private Sector) Act 2000. Red Oxygen is not allowed to use or sell any of the data from text messages that are sent through their systems. Text messages are considered phone calls and the use or sell of these messages would be considered wiretapping. More of Red Oxygen's privacy policy can be reviewed at http://redoxygen.com/privacy-policy/.

**F.3.f. Management of HIV seroconversion and STI diagnosis during the course of the study.** After initial enrollment and intervention completion, if a participant reports an HIV seroconversion on the questionnaires he will still be eligible to participate in subsequent assessments. Participants who report seroconversion during the study will be referred for care at one of our community partners or appropriately referred elsewhere if he requests. Each site coordinator will maintain lists of referrals and will assist in making linkages to care.

With regard to STI testing and diagnosis:

- All participants will be tested for Gonorrhea and Chlamydia at baseline and post-intervention (12 month follow-up). Participants who test positive at baseline will also be tested at 3 month and 6 month follow-ups in addition to the 12 month follow-up.
- For participants who complete STI testing at a CDPH clinic, CDPH clinic staff will contact participants with their STI test results. For those who are positive for Chlamydia or Gonorrhea, CDPH clinic staff will report the results to the state or local health department. Clinic staff will also make sure that participants receive appropriate medical attention.
- Participants who complete STI testing at home, at a university site, or at a CDPH clinic will be sent an encrypted email that they can only open using their unique study ID to receive their STI test results. Participants may speak to Keep It Up! study staff if they have any questions or concerns about their results. For those who are positive for Chlamydia or Gonorrhoeae, Keep It Up! study staff are required to report the results to state or local health department. Research study staff will follow up with the client to be sure they receive appropriate medical attention. Research staff is also available for questions or concerns regarding STI diagnosis and may provide referrals to local treatment centers. The ability to link YMSM to needed clinical services is a distinct strength of this proposal as the multi-disciplinary investigative has considerable experience doing research with high-risk youth populations and the program of research is embedded in a larger network of CBOs designed to meet the needs of LGBT youth and YMSM.
- Participants who live abroad at the time of their 12 month STI test and complete testing outside of the U.S. will receive their STI results from their healthcare provider. For those who are positive for Chlamydia or Gonorrhea, the healthcare provider will be responsible for reporting the results to the appropriate health department. The healthcare provider will also be responsible for providing participants with or referring them to appropriate medical attention.

**G. Trial Efficacy**

**G.1. Plan for interim analysis of efficacy data and trial stopping rules.**

Ongoing efforts will be made to ensure that the intervention is not causing harm. The DSM Board will conduct interim analyses after approximately half of the participants have completed each follow-up assessment. The DSM Board will convene, either in person or via conference call, to examine the data and check to see if either condition is resulting in deleterious effects, as indicated by significant increases in risky sexual practices or substance use.

The NU IRB has the authority to suspend or terminate approval of any research at its site that has been associated with unexpected serious harm to participants. The conditions under which the study would be

stopped include, but are not limited to, a direct causal link between the study conditions and the hospitalization, impairment, or death of any research participants.

**H. DSM Plan Administration**

**H1. Responsibility for Data and Safety Monitoring.**

The overall responsibility for data and safety monitoring lies with Dr. Mustanski. As PI, he is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events. Any unexpected or SAEs that occur during the course of the study will be reported by the PI to the NU IRB in accordance with current University guidelines for reporting adverse events. The PI will regularly review all data related to adverse events. The PI, Co-Is, and study staff will teleconference on a monthly basis to discuss enrollment, retention, and safety of study participants.

**H2. Frequency of DSM.**

Information related to recruitment, enrollment, and retention will be relayed to the DSMB every six months, unless the Board requests otherwise.

**H3. Content of DSM report.**

The project staff will prepare an annual report which will include: (1) a brief description of the trial; (2) baseline sociodemographic characteristics; (3) retention and disposition of study participants; (4) QA issues; (5) regulatory issues; (6) AEs; (7); SAEs; and (8) efficacy.

**I. DSMB Plan**

In accordance with the National Institutes' of Health requirement that multisite clinical trials have Data and Safety Monitoring Boards (DSMB), we will establish a DSMB according to policies and requirements put forth by NIH. Specifically: (1) the DSMB must include a minimum of 3 individuals; (2) board members must have no direct involvement with the intervention or study and no other conflict of interest with the intervention or study; (3) the board must meet at least two times per year during periods when intervention and/or data collection are taking place and at least once per year during other phases (e.g., developmental phase or analysis phases).

Dr. Mustanski, the PI, has served on numerous DSMBs for HIV prevention trials and is familiar with their organization and operation. The Northwestern University Clinical and Translational Sciences Institute (NUCATS) will assist in establishing protocols for managing the DSMB. The proposed study is considered to present minimal risk to participants given that subjects will complete questionnaires, receive STI tests, and participate in a behavioral intervention.

**I.1. Members and affiliations**.

The DSMB will initially include three members who have agreed to serve in this capacity and will provide expertise in eHealth approaches to HIV prevention, research with the target population of diverse YMSM, and the design and analysis of HIV prevention trials. Members of the DSMB will disclose any potential conflicts of interest, either pre-existing or those that develop during their tenure, to the PI and the NIMH Project Officer. All DSMB members will be voting members and will be appointed for the life of the project and each member of the DSMB will sign a statement of confidentiality.

The DSMB will be chaired by Dr. Sheana Bull of the University of Colorado School of Public Health Division of Community and Behavioral Health. In the past decade Dr. Bull has focused on the development and testing of behavioral interventions for health promotion using technology. She is involved in HIV prevention projects utilizing mobile phones and text messaging, social networking sites and the Internet. Dr. Jose Bauermeister of the University of Michigan School of Public Health Division of Health Behavior & Health Education will serve as a DSMB member. Dr. Bauermeister's research focuses on sexuality and health, and interpersonal prevention and health promotion strategies for high-risk adolescents and young adults. He is Principal Investigator of several projects examining HIV/AIDS risk among young men who have sex with men (YMSM). Dr. Michael Hudgens of the University of North Carolina at Chapel Hill Department of Biostatistics will also serve as a DSMB member. He is the Director of the Biostatistics Core of the UNC Center for AIDS Research and has served as lead statistician on multiple clinical trials for prevention of HIV sponsored by the NIH and CDC.

**I.2. Frequency of meetings.**
The DSMB will conduct an open session prior to the initiation of the trial. The DSMB will have been provided with all material associated with the trial, and have had sufficient opportunity to review the documents. At the open session all members will discuss any potential concerns for the safe and effective conduct of the impending study. With data collection beginning in Year 1, DSMB meetings will be held every 6 months. However, the Chair of the DSMB can call a meeting as needed. Serious adverse events will be reported to the Chair as soon as they occur. The Chair of the DSMB will determine whether an in-person meeting or teleconference is needed. Prior to the meetings, a written report containing any outcome data will be sent to DSMB members by the study statistician. Each meeting will be divided into three parts. (1) There will be an open session in which the PI will be present to review the progress of the study and to answer questions from members of the DSMB. (2) A closed session involving the DSMB members and the study statistician will be held during which outcome results will be discussed. (3) A final session involving only the DSMB members will be held to discuss the progress of the study and the outcome results, to develop recommendations, and to takes votes as necessary.

**I.3. Conflicts of interest.**
Members of the DSMB will disclose any potential conflicts of interest, either pre-existing or those that develop during their tenure, to the PI and the NIDA PO.

**I.4. Protection of confidentiality.**
Member of the DSMB will protect the confidentiality of the trial data and the monitoring results.

**I.4. Monitoring activities.**
**I.4.a. Members of the DSMB** will perform the following activities: (1) review the research protocol and plans for data and safety monitoring; (2) review progress of the trial, including analysis of data quality and timeliness; subject recruitment, randomization and retention; subject risk versus benefit; and other factors that may affect outcome; (3) review SAE reports, provide commentary, and provide oversight to ensure that reports are relayed to individual IRBs and to the Office of Human Research Protections, as indicated; (4) review analyses of outcome data of the proposed study and review reports of related studies; (5) determine whether the trial should continue as designed, should be changed, or should be terminated based on the data and make recommendations to the NIH, Institutional Review Boards, and investigators considering conclusion or continuation of the study; (6) review proposed modifications to the study prior to their implementation; (7) protect the confidentiality of the trial data and the results of the monitoring; (8) determine whether and to whom outcome results should be released prior to the reporting of study results; (9) following DSMB meetings, provide appropriate NIH staff and the PI with written information concerning their findings.

**I.4.b. The PI, Dr. Mustanski,** will be responsible for the following**:** (1) preparation and establishment of a plan for the data and safety monitoring; (2) evaluation of all members of the DSMB for a conflict of interest or financial stake in the outcome of the trial; (3) delegation of the ongoing monitoring of the trial to the DSMB; (4) ensuring that monitoring is timely and effective and that the DSMB is composed of individuals with appropriate expertise to accomplish their assigned tasks; (5) overseeing the monitoring activities; (6) responding to and addressing recommendations that result from monitoring activities; (7) provision of adverse event reports and other safety data to the DSMB, as well as any changes in the trial or annual reports to the IRB and NIDA; (8) contributing to the report that the DSMB generates, which will be distributed to the IRB and NIDA; (9) submitting the DSMB report to the IRB.

**I.5. Communication plan to IRB and NIDA.**
Dr. Mustanski will promptly inform NIDA and the IRB of any changes in recruitment or in the protocol relevant to safety as the study is being performed. He will additionally notify NIDA of any actions taken by the IRB during continuing study review and of any major changes in the status of the ongoing protocol which would only occur with IRB approval. Such changes would include, but are not limited to: (1) amendments to the protocol; (2) temporary suspension of patient accrual, or of the protocol; (3) changes in informed consent or

IRB approval status; (4) termination of participant accrual or of the protocol; or (5) other problems or issues that could affect the human subjects in the study.