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ATN 141 - MyChoices:
Mobile-Based Application to Increase Uptake of HIV Testing, Detection of New HIV Infections, and Linkage to Care and Prevention Services by Young Men who have Sex with Men

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SIGNATURE PAGE

I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., US National Institutes of Health, Division of AIDS) and institutional policies.

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AC	Analytic Core
AE	Adverse Event
AIDS	Acquired Immunodeficiency Syndrome
ATN	Adolescent Medicine Trials Network for HIV/AIDS Interventions
ARBA	AIDS Risk Behavior Assessment
BAA	Business Associate Agreement
CASI	Computer Assisted Self-Interview
CFR	Code of Federal Regulations
CRF	Case Report Form
DHHS	U.S. Department of Health and Human Services
EC	Ethics Committee
GCP	Good Clinical Practices
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IRB	Institutional Review Board
LGBT	Lesbian, Gay, Bisexual, and Transgender
MC	Management Core
NICHD	National Institute of Child Health and Development
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
PI	Principal Investigator
PrEP	Pre-Exposure Prophylaxis
OHRP	Office of Human Research Protection
QNS	Query and Notification System
QR	Quick Response (Code)
QA	Quality Assurance
RCT	Randomized Controlled Trial
RDC	Remote Data Capture
SAE	Serious Adverse Event
SCT	Social Cognitive Theory
SID	Study Identification Number
SMART	Study Management and Retention Tool
SMS	Short Message Service
SOC	Standard of Care
SRV	Subject Recruitment Venue
SUS	System Usability Scale
TC	Technology Core
UAE	Unanticipated Adverse Event
UNC- CH	The University of North Carolina at Chapel Hill
YMSM	Young Men who have Sex with Men

STUDY ABSTRACT

DESIGN:	"MyChoices", an app developed using iterative feedback from youth, will be refined through theater testing in focus groups (Aim 1) and an open technical pilot (Aim 2) with young men who have sex with men (YMSM) at iTech SRVs in Boston, MA, Bronx, NY, Chapel Hill, NC, and/or Atlanta, GA. To plan for an R01 efficacy trial proposed for years 3-5 of the current iTech project, we will conduct a pilot randomized controlled trial (Aim 3) to assess acceptability, feasibility, and preliminary efficacy of MyChoices.
DURATION:	Aim 1: single study visit (focus group) for theater testing Aim 2: 2 months Aim 3: 6 months
SAMPLE SIZE:	Aim 1: Up to 40 YMSM across two iTech SRVs Aim 2: Up to 15 YMSM across two iTech SRVs Aim 3: Up to 60 YMSM across two to four iTech SRVs (~15 to 30 per SRV)
POPULATION:	● Between 15 and 24 years of age ● HIV uninfected (or HIV status unknown) ● Assigned male sex at birth and identifies as male ● Have not had an HIV test within past 3 months (for Aims 2 and 3) ● Not currently on PrEP regimen (for Aims 2 and 3) ● High-risk for acquiring HIV via sexual transmission ● Own or lease Android mobile phone (for Aims 2 and 3) ● Able to understand, read, and speak English
STRATIFICATION:	Participants in Aim 3 will be randomized 2:1 to receive the MyChoices app vs. Standard of Care
DATA COLLECTION:	Aim 1: Focus groups will be audio-recorded and participants will complete a brief demographic questionnaire.

Aim 2: At enrollment and study completion, participants will complete a brief quantitative assessment (in person at baseline and online at follow-up); online qualitative exit interviews will be conducted; and app usage patterns will be assessed.

Aim 3: At Month 3 and Month 6 after enrollment/baseline, all participants will complete a brief quantitative assessment (in person at baseline and online at follow-up) and app usage patterns will be assessed. An online qualitative exit interview will be conducted for up to 20 participants.

OBJECTIVES

1) To refine a mobile phone app, “MyChoices,” to promote HIV/STI testing and PrEP uptake among YMSM by conducting theater testing with up to 40 YMSM. Data will be used to make final app refinements.

2) To conduct a technical pilot with up to 15 YMSM to optimize MyChoices app functionality, technical performance, and user satisfaction. Data will be used to finalize the pilot study methods, the mobile app functionalities, and measures for the pilot trial (Aim 3).

3) To conduct a pilot randomized controlled trial (RCT) with up to 60 YMSM to evaluate the feasibility and acceptability of MyChoices to increase HIV/STI testing and PrEP uptake among YMSM.

1.0 INTRODUCTION

1.1 Background

HIV incidence is growing most rapidly among young men who have sex with men (YMSM) in the United States (US). Moreover, among all MSM, YMSM account for 15% of new infections.[1] Awareness of HIV status through routine HIV testing is essential for reducing the population burden of disease, as well as for improving health outcomes for those who are infected.[3-5] However, it is estimated that, compared to the general population, a higher proportion of YMSM (13% vs. 44%, respectively) living with HIV do not know that they are infected. HIV-infected black YMSM are 33% less likely to be aware of their HIV status.[6, 7]

HIV testing among young adults is suboptimal. Data suggest that approximately 60% of YMSM do not get annual HIV tests.[19] The normal developmental trajectory of adolescence and young adulthood involves behavioral experimenting, risk taking, and confronting a host of difficult choices with regard to identity formation.[20] These age-appropriate behaviors, beliefs of invincibility, and still developing cognitive processes[21] may play a role in increasing HIV risk-taking behaviors and placing a low priority on HIV testing.

The ongoing and growing HIV risk for YMSM highlights the need to reach younger individuals using developmentally appropriate, innovative methods and modalities. In addition to expanding access to effective prevention modalities, innovative methods to reach YMSM "where they are" must be developed. Smartphone use is nearly universal among youth in the US.[15] Younger adults, racial and ethnic minorities, and socioeconomically disadvantaged populations have been identified as having high rates of smartphone use, reducing concerns of inequitable access to the technology.[16] The use of mobile phone applications ("apps") is ubiquitous, and is a common way in which youth interact, get information, and meet sex partners. As such, mobile apps offer unique opportunities for public health interventions, including efforts to increase HIV testing, particularly for YMSM, who may be open to receiving information in a familiar and discreet environment.

Although the popularity of mobile health apps (mHealth) is growing, there are limited data on the efficacy of app-based interventions to enhance HIV prevention and increase HIV testing among MSM, particularly YMSM. However, formative research suggests that online, mobile, or social media outlets are acceptable and feasible means to increase uptake of prevention services and HIV testing among MSM.[10-14] Informed by extensive formative research, Dr. Patrick Sullivan of Emory University, with app developers from Keymind, developed and tested an HIV testing promotion app for adult MSM ("HealthMindr"). Our initial formative research with YMSM suggested interest in an HIV testing app, like HealthMindr, but the youth agreed that it had to be adapted to be more culturally and developmentally appropriate for their peers.

1.2 Rationale

Advances in mobile phone technologies have enabled YMSM to have immediate access to broad social and sexual networks. The proposed project responds to the increasingly widespread use of mobile technology in the US. A recent review of the literature demonstrated that most mobile phone apps for HIV prevention are designed by non-academic, non-public health developers and are not guided by behavior change theories.[24] Moreover, only a small

proportion of available HIV prevention mobile apps specifically address MSM populations, and none was developed specifically for YMSM.[24]

Using HealthMindr as a starting point, our interdisciplinary team of HIV clinicians, epidemiologists, behavioral scientists, and app developers designed the "MyChoices" app by conducting formative work with YMSM in Boston, Chicago, and Los Angeles. MyChoices is informed by the Social Cognitive Theory (SCT) which specifies a core set of factors that influence health behavior with an emphasis on goal setting, self-efficacy, and self-regulation.[22, 23] SCT holds that cognition, behavior, and environmental influences interact and are reinforcing. For example, self-regulatory functions (e.g., self-monitoring one's HIV testing) and self-efficacy (e.g., belief that one can attain the goal to test regularly) are enhanced by facilitative environmental conditions,[22, 23] such as reminder systems. "MyChoices" uses interactive capabilities and environmental influences to support self-regulation and self-efficacy by enhancing the feeling of control over one's ability to get tested regularly for HIV. For example, the app allows users to create an individualized HIV testing plan where youth are encouraged to select predetermined built in reminders which will alert them when it is time to get tested. The geofencing technology allows a user to be notified when they are near a testing location and when they are due for HIV testing. These techniques are expected to help overcome key barriers to HIV testing (e.g., being perceived as inconvenient), which we anticipate will increase self-efficacy and self-regulation, and consequently, change behavior.

This study will provide the necessary data to make final refinements to the intervention in preparation for a multi-city, RCT of this app and another youth-optimized app ("LYNX") versus standard of care among YMSM in Years 3-5 of the proposed iTech award period. If shown to be efficacious, to our knowledge, "MyChoices" will be the first comprehensive HIV prevention app designed specifically for YMSM. We anticipate that MyChoices will increase HIV testing and linkage to prevention services because it is developmentally appropriate and meets YMSM where they are, in an environment that is familiar and discreet.

2.0 STUDY OBJECTIVES

2.1 Primary Objectives

Aim 1, Qualitative research for final app refinement (Months 1-9). To refine and enhance "MyChoices" components and to include additional components to increase PrEP uptake among YMSM, we will conduct qualitative research based on interactions with the current app (i.e., "theater testing") with up to 40 YMSM in 2 SRV sites (~2 groups at each SRV). YMSM of color will be oversampled in order to reach a target enrollment of approximately 50% and ensure sufficient representation in the population with the most need. We will demonstrate the current mobile app to participants and elicit feedback on: the overall appearance and functionality of the interface, appeal, and usability; ways to maximize acceptability; components that they like and/or dislike; and areas for improvement. Guided by the SCT model, we will elicit feedback on the following areas designed to increase PrEP uptake among YMSM: 1) potential content to address PrEP-related self-regulation (e.g., recommendations to speak with a provider about PrEP if their risk assessment indicates potential eligibility, and how their risk may be impacted if they take PrEP); 2) content and functionalities to improve PrEP use self-efficacy [e.g., videos showing couples discussing PrEP, GPS-enabled provision of links to local PrEP providers which allows them to manage their own PrEP care, and guidance on questions to ask providers about PrEP (e.g., dosing, side effects, necessary follow-up]); 3) potential content to address

environmental influences on PrEP uptake (e.g, information on insurance and other payment options for PrEP). We will ask participants about attitudes regarding documenting their testing practices and results through signed medical releases, sending photos of test results, and/or scanning a Quick Response (QR) code (i.e., barcode that is scanned at a testing site to "check in") to document completed testing, for feasibility testing in the pilot RCT. Theater testing groups will last 60-90 minutes, and discussions will be audio recorded and transcribed verbatim. Facilitators will also take notes and complete standardized debriefing forms immediately following the visit so that data can be used in real-time to refine the app.

Aim 2, Technical Pilot (Months 10-12). After refinement according to Aim 1 findings, the "MyChoices" app and intervention procedures will be evaluated and revised during a 2-month technical pilot with a small group of YMSM participants (up to 15 YMSM at two iTech sites). All participants will be given brief instructions on the purpose of the "MyChoices" app and an overview of how to use it. They will complete a brief online assessment (see Measures) at baseline and at the end of the 2-month follow up period. Participants will also be asked to provide feedback during exit interviews conducted by study staff online using VSee technology (described fully below) on functionality, technical performance, errors and bugs encountered, overall experiences using the app, and feedback for further refinement. These data will be used to refine the app, intervention protocol, and instruments to be tested in the pilot RCT (Aim 3).

Aim 3, Pilot RCT (Months 13-24). We will conduct a feasibility and acceptability study of the app and evaluation of the app and its components for preliminary efficacy. This information will determine whether MyChoices moves forward to be tested in an efficacy trial in years 3-5 of the current iTech. We will enroll up to 60 YMSM across two to four iTech SRVs and randomize them to receive either 1) the "MyChoices" app and provision of referrals to local HIV/STI testing and PrEP resources (n=40); or 2) provision of referrals to local HIV/STI testing and PrEP resources (i.e., SOC) (n=20). Participants will be followed for 6 months and will complete a brief online assessment every 3 months. At 3 months post enrollment, all participants who seroconvert and up to 20 participants randomized to the intervention arm will also be asked to provide feedback during qualitative interviews conducted by study staff online using VSee technology (described fully below) on functionality, technical performance, errors and bugs encountered, overall experiences using the app, and feedback for further refinement.

2.2 Study Hypotheses/Research Questions

Primary Objectives:

Aim 1: To conduct qualitative, formative work to refine a mobile phone app, MyChoices, to promote HIV/STI testing and PrEP uptake among YMSM

Aim 2: To conduct a technical pilot to optimize MyChoices app functionality, technical performance, and user satisfaction

Aim 3: To conduct a pilot RCT to evaluate the feasibility and acceptability of MyChoices to increase HIV/STI testing and PrEP uptake among YMSM

Aim 3 Secondary Objectives:

To compare the rate of HIV/STI testing in the MyChoices intervention vs. control arms

To compare the rate of PrEP uptake in the MyChoices intervention vs. control arms

To compare changes in sexual risk behaviors among YMSM in the MyChoices intervention vs. control arms

Study Hypotheses/Research Questions

Aim 1: Is the MyChoices *app appealing to YMSM? What changes should be made to make it more acceptable to YMSM?*

Aim 2: Are the MyChoices *app and study procedures and documents primed to be tested in a pilot trial?*

Aim 3: Is the MyChoices *app a feasible and acceptable method to increase HIV testing and PrEP uptake among YMSM? Are there differences in HIV/STI testing and PrEP uptake among participants who receive* MyChoices *vs. the standard of care?*

The MyChoices *app will be highly feasible and acceptable among YMSM aged 15-24.*

The MyChoices *app will have preliminary efficacy in increasing HIV/STI testing and PrEP uptake.(secondary objective)*

3.0 STUDY DESIGN

MyChoices app was developed through an iterative process of app development. In the current study, “MyChoices” will be further refined through theater testing with ~ 4 focus groups with up to 40 YMSM (Aim 1) and an open technical pilot (Aim 2) with up to 15 YMSM at two iTech SRVs (Boston and Bronx). To plan for an R01 efficacy trial proposed within the current iTech project, we will conduct a pilot RCT with up to 60 YMSM (Aim 3) to assess acceptability, feasibility, and preliminary efficacy of MyChoices at iTech SRVs at Boston, Bronx, Chapel Hill, and/or Atlanta.

Aim 1: Theater Testing Focus Groups

To refine the “MyChoices” app and enhance components designed to increase PrEP uptake among YMSM, study staff at each SRV will conduct theater testing with up to 40 YMSM in up to four focus groups (~2 groups and up to 10 YMSM per group at each SRV). We will demonstrate the mobile app to participants and elicit feedback on the app. Theater testing focus groups will last 60-90 minutes, and discussions will be audio recorded and transcribed verbatim by the Analytic Core (AC).

Aim 2: Open Technical Pilot

After refinement according to Aim 1 findings, the "MyChoices" app and intervention procedures will be evaluated and revised during a 2-month open technical pilot with a small group of YMSM participants (up to 15 YMSM at 2 iTech sites). All participants will be given brief instructions on the purpose of the "MyChoices" app, how to access it and an overview of how to use it, including reviewing privacy settings, completing an initial risk assessment as well as an initial HIV testing plan. Participants will be encouraged to explore all components of the app and to use it routinely. They will complete a brief online assessment (see below) at baseline and at the end of the 2-month follow-up period. Participants will also be asked to provide extensive feedback during exit interviews conducted online by study staff at Fenway Health using VSee technology (described fully below) on functionality, technical performance, errors and bugs encountered, overall experiences using the app, and feedback for further refinement.

Two quantitative assessments will be conducted with each participant at baseline and 2-months follow-up. The participant will complete a Computer Assisted Self-Interview (CASI) survey, which includes questions and feedback pertaining to the acceptability and utility of the app, and assess how the app and intervention components could be strengthened, identifying areas needing improvement for future iterations. Participant feedback will be specifically sought on the subjective impact of the app on increased HIV testing and PrEP uptake among YMSM. Participant feedback will also be solicited on the acceptability of the assessments with respect to duration and relevance.

Qualitative data will be obtained from all participants through brief exit interviews using VSee software. A developed interview guide will gather information from participants: 1) acceptability and utility, 2) assess how the app and intervention components could be strengthened, 3) identify areas needing improvement for future iterations, and 4) the acceptability of the assessments with respect to duration and relevance.

Exit interviews will last approximately 30 minutes. Study team members at Fenway Health who conduct the interviews will document the feedback on the Exit Interview Summary CRF during the online interview, and review them with study investigators during weekly team meetings.

Participants who seroconvert during Aim 2 (two month technical pilot) will be offered a referral for HIV care, including confirmatory HIV testing and linked to HIV care if confirmatory testing is positive; continue to have access to the app, and be invited to complete the 2-month follow up CASI assessment and the exit interview. A referral for linkage to care will be offered by the SRV clinic. A set of questions will be asked regarding the participant's experience, particularly as it pertains to app use and linkage to care.

Aim 3: Pilot Randomized Controlled Trial (RCT)

Approximately 60 YMSM recruited from 2 to 4 iTech SRV sites (~15 to 30 at each SRV) will be enrolled and randomized (2:1) to one of two conditions: a) Intervention arm: download the MyChoices app and provided links to local HIV/STI testing and PrEP resources (n=40); or b) Control arm: an initial provision of links to local HIV/STI testing and PrEP resources (n=20). Individuals will then be followed for 6 months. The primary outcomes will be feasibility and acceptability of the app among participants in the intervention arm at 3 month follow up. Secondary outcomes will be preliminary efficacy of the app to increase HIV and STI testing (via self-report) and PrEP uptake (via self-report) by comparing rates of each at follow up timepoints. Additionally, every 3 months, participants will complete a brief online quantitative assessment to

measure sexual behavior, HIV testing patterns, linkage to PrEP and other prevention services, HIV/STI test results, and general health care access. Among those in the experimental condition, we will track usage patterns to assess frequency of use of specific app functionalities. At 3 months post enrollment, all participants who seroconvert (regardless of study arm) and up to 20 participants in the intervention arm will also be asked to provide extensive feedback during interviews conducted online by study staff at Fenway Health using VSee technology (described fully below) on functionality, technical performance, errors and bugs encountered, overall experiences using the app, and feedback for further refinement.

Participants will be selected for interviews using purposive sampling based on level of engagement with the app, whether participants completed HIV/STI testing and/or initiated PrEP during the study, and to achieve diversity based on sociodemographics (e.g. age, race/ethnicity). Additionally, we will offer interviews to all participants who have a confirmed HIV diagnosis. In addition to asking about their experiences using the app, these participants will also be asked about additional information or support that would have been helpful at the time of receiving a positive HIV test result, and their experiences in getting linked to HIV care. By purposively sampling certain participants for the exit interviews, the goal is to select "information-rich cases from which one can learn a great deal about issues of central importance to the purpose of the research."[76]

For the pilot RCT, there will be three major assessment points: Baseline, 3-month, and 6-month post-baseline. Baseline assessments will be conducted in-person at the SRV. Participants can choose to do follow up assessments remotely or in person. At each major assessment, participants will complete an assessment battery via a secure web-based data entry system, which is guided by the SCT model and based on our formative work and prior experience; however, the final list of measures will be determined during the open pilot.

Qualitative data will be obtained from participants through brief interviews using VSee software. A developed interview guide will gather information from participants: 1) acceptability and utility, 2) assess how the app and intervention components could be strengthened, 3) identify areas needing improvement for future iterations, and 4) the acceptability of the assessments with respect to duration and relevance.

Exit interviews will last approximately 30-60 minutes. Study team members at Fenway Health who conduct the interviews will document the feedback on the Exit Interview Summary CRF during the online interview, and review them with study investigators during weekly team meetings.

The primary outcomes will be:
Acceptability. To measure acceptability of the "MyChoices" app, the System Usability Scale (SUS)—a validated 10-measure scale that assesses subjective usability of a system, or, in this case, an app—will be assessed through the quantitative survey at the follow up time points. It is scored from 0 to 100, and a score of 50 or greater indicates that the app is acceptable.

Feasibility. To determine feasibility, we will use app analytics to determine whether at least 60% of individuals randomized to the intervention condition opened the "My Choices" app at least one time after their initial introduction to the app by research staff by the 3-month follow up assessment. We will also assess the proportion of participants who complete their HIV testing plan (regardless of testing intervals)—a primary function of the app.

Secondary outcomes will be:
***Preliminary Efficacy*.**

- *HIV and STI testing frequency*
  - Self-repored HIV testing
  - Self-reported STI testing
  - Paritcipants will be asked about frequency and results of all HIV/STI tests
  - Participants will be asked to sign medical release forms for the release of their testing results from the respective testing site so that study staff can collect official results through medical record abstraction
- *PrEP interest and uptake*
  - *PrEP care linkage: participants will self-report whether, in the past 3 months, they made and attended a clinic appointment for PrEP initiation, whether they were prescribed PrEP, and whether they utilized PrEP.*

3.1 Study Population

For all aims of the study, participants will be HIV uninfected YMSM between ages 15 and 24 and self-report evidence of high risk for acquiring HIV infection.

YMSM of color will be oversampled in order to reach a target enrollment of approximately 50% and ensure sufficient representation in the population with the most need. Oversampling will be accomplished by focusing efforts on venues more likely to be frequented by YMSM of color. The recruitment strategies can be adaptive over the enrollment period to help ensure the specified targets.

3.2 Sample Size

Aim 1: Theater Testing Focus Groups
We will conduct theater testing with up to 40 YMSM in up to four groups at 2 iTech SRV sites.

Aim 2: Open Technical Pilot
The “MyChoices” app and intervention procedures will be evaluated and revised during a 2-month open technical pilot with up to 15 YMSM at 2 iTech SRV sites.

Aim 3: Pilot Randomized Control Trial
Approximately 60 YMSM in 2-4 iTech sites (~15 to 30 at each site) will be enrolled and randomized (2:1) to one of two conditions: a) download the app and provided links to local HIV/STI testing resources (n=40); or b) an initial provision of links to local HIV/STI testing resources (n=20). Randomization is site-specific and stratified by age (15-18, 19-24).

4.0 SELECTION AND ENROLLMENT OF STUDY PARTICIPANTS

4.1 Inclusion Criteria

For Aim 1 only

- Age 15 to 24 years
- Assigned male sex at birth
- Identify as male
- Self-report being HIV uninfected or HIV status-unknown at screening
- Self-report at least one episode of anal intercourse with a male partner during the last 6 months
- Able to understand, read, and speak English
- Own or lease an Apple (iOS) or Android mobile phone

For Aims 2 and 3

For Aims 2 and 3

- Age 15 to 24 years.
- Assigned male sex at birth and male identified.
- Self-report being HIV uninfected or HIV status-unknown at screening.
- Self-report having not had an HIV test in the past 3 months (for Aims 2 and 3 only).
- Self-report not currently taking PrEP (for Aims 2 and 3 only).
- Participants ages 15-18: self-report at least one episode of anal intercourse with a male or transfemale partner during the last 6 months.
- Participants ages 19-24: self-report evidence of high risk for acquiring HIV infection including at least one of the following:
    - at least one episode of condomless anal intercourse with an HIV-infected or unknown HIV status male or transfemale partner during the last 6 months; or
    - anal intercourse with 2 or more male or transfemale sex partners during the last 6 months; or
    - exchange of money, gifts, shelter, or drugs for anal sex with a male or transfemale partner during the last 6 months; or
    - sex with a male or transfemale partner and has had an STI during the last 6 months.
- Able to understand, read, and speak English.
- Owns or leases a phone with Android platform (for Aims 2 and 3) or iOS platform (Aim 3 only), and has an active data plan

4.2 Exclusion Criteria

- Currently enrolled in another HIV intervention study.*
- Prior enrollment in an HIV vaccine trial with receipt of experimental vaccine product.*
- Enrollment in earlier aim of MyChoices study**
- Any medical, psychiatric, or social condition or other responsibilities that, in the judgment of the investigator, would make participation in the study unsafe, complicate

interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

- Not willing and/or not able to download the MyChoices application

**These criteria are only for the technical pilot and pilot RCT.*

Individuals who participated in a focus group for Aim 1 ARE eligible to participate in the open pilot for Aim 2, provided they meet all other eligibility criteria. Individuals who participated in a focus group for Aim 1* ***and/or the technical pilot in Aim 2 *ARE NOT eligible to enroll in the Aim 3 pilot RCT.*

4.3 Recruitment

Active recruitment will be carried out by study staff at iTech SRVs (Fenway Health in Boston, MA, the Children's Hospital at Montefiore in the Bronx, New York, UNC-CH in Chapel Hill, NC, and/or PRISM Health at Emory University in Atlanta, GA) by recruiting individuals at organizations and venues where YMSM attend, including STI clinics, community-based organizations for LGBT youth, events, etc. At recruitment venues, trained recruiters will approach youth and offer them information about the study (either verbally or by offering them a business card or advertisement flyer), including brief descriptions of the study design and contact information (study email and phone number). Youth may also choose to complete an online eligibility screener during in-person recruitment. For Aim 3 (pilot RCT), we will follow respondent-driven sampling (RDS) methods and use a long-chain referral method to supplement recruitment, especially with the adolescents (15-17) who may be harder to reach than young adults (18-24).

Additionally, passive approaches for recruitment will include posting study information via flyers, posters, and palm cards describing the study at these venues. Moreover, online recruitment will be conducted, with the support of the iTech Technology Core, using popular online social media outlets (e.g., Facebook, Grindr, etc.). These efforts have been successful in other projects with this population, and as such, we do not anticipate having problems reaching our target sample.

Potential subjects will be approached by trained clinic staff at participating sites. They will be informed of the nature of the study, the information to be collected, and the evaluations and assessments that are involved. Those who express interest in the study will be required to provide informed consent or assent and have eligibility criteria confirmed by study staff before enrolling into the study.

All recruitment materials will be submitted to the UNC-CH IRB as the single IRB (IRB of Record) with a description of intended use for approval prior to use.

4.4 Informed Consent

Informed consent/assent. The informed consent process will occur on the day the enrollment visit is held. Interested persons will be guided through the informed consent process by study staff, who will explain all study procedures, answer questions concerning the study and consent

process, and offer a copy of the informed consent/assent form. The research staff member will give the participant as much time as needed and will address any questions or concerns they may have. The participant will be allowed to take the consent/assent form home and review it before enrolling in the study if the participant needs more time to review the form. The research staff member will ask the participant questions to gauge comprehension. The consent/assent form describes all study procedures, including confidentiality and privacy, information about potential risks, discomforts, benefits of participation, and information regarding who they can contact with further questions. It also states that participation is voluntary, that participants may decide not to take part or to withdraw from the study at any time without penalty or loss of any benefit to which they might otherwise be entitled, and that study participation is in no way related to being able to access or continue getting care or services at any participating study site. Participants can refuse to answer any question, and can withdraw from the study at any time. The PIs, Co-PIs, or designee at each site will review all informed consents and assents.

Assessing for decisional capacity. For all participants, the research assistant (RA) reviews the informed consent/assent to make an assessment of the youth's decisional capacity and ability to provide consent/assent prior to signing, using a 2-step process. First, the RA determines if the person understands the study goals by asking "Can you tell me what this study is about?" In step 2, potential participants will be asked questions designed to assess their capacity to understand, appreciate, reason with, and express a choice about participation in our specific protocol. Participants will be asked to: name things they will be expected to do during the study; explain what they would do if they no longer wished to participate in the study**;** explain what they would do if they experienced distress during the study; and identify potential risks for participating in the study. For youth who cannot answer these questions, the RA will go back and review the relevant elements of consent with the participant again and repeat the process. Youth who appear not to understand after repeated review will not be enrolled in the study.

Waiver of parental consent. We will request that the UNC-CH IRB as the single IRB (IRB of Record) grant a waiver of parental consent to participate in this research study for youth participants who are 15 to 17 years of age. The research team has been granted waivers of parental permission for prior studies with sexual minority youth. Under 45 CFR 46.408 (c), an IRB has the authority to waive parental permission if it determines that "a research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects" and "an appropriate mechanism for protecting the children who will participate as research subjects is substituted" and "that the waiver is not inconsistent with Federal, State, or local law." A waiver of signed consent and parental/legal guardian permission will be sought given that minor individuals can often seek sexually transmitted infection (STI) and HIV testing without parental/legal guardian permission, depending on each site's state laws, and given that many of the youth in our study are likely to be gender and/or sexually fluid or have an attraction to persons of the same gender, but may not be out to their parents; requiring parental permission may place participants at risk for outing themselves as part of the LGBT community or being at risk for HIV infection. A waiver of parental permission for studies with LGBT youth that do not involve greater than minimal risk is a common practice among researchers working in the area of gay and lesbian health/mental health. This is done to avoid the selection biases operating in only recruiting youth whose parents are both aware of and comfortable with their sexual orientation. Commonly, these youth have explored their sexual orientation without their parents' knowledge as the youth struggle with issues of disclosure and its consequences within the social, religious, and economic context of their families. A

requirement for parental permission in this type of study could not only affect a person's willingness to participate, but could also potentially impact the ability of researchers to engage in this type of research with sexual minority youth.

If the purpose of requiring parental permission as stated in CFR is to protect the minor subject, then requiring parental permission for youth in these circumstances is not a reasonable requirement. Additional privacy protections are provided in that all assessments, notes, reports, and other records will be identified by only a coded number to maintain participant confidentiality. These records and any forms that do contain identifying information (e.g., consent/assent forms, contact information) will be kept in a locked, limited access area (such as a locked file cabinet) at the participating site.

4.5 Screening

All potential participants (whether recruited online or in-person) will complete an online screening survey to obtain consent/assent to be screened and verify all inclusion criteria. Screening may occur on the same day as enrollment or beforehand. The online screening survey will begin with a script that will be read by participants to explain the purpose of screening and clarify that if they are eligible, they will be invited to participate in the study. The script will also provide general information about the research study, the nature of the screening questions and related potential risks, the approximate length of the screening (~5 minutes), the confidentiality of the screening information, the use of any screening information obtained, the ability to skip any questions or withdraw at any time, and contact information of key study personnel. After reading this screening script, participants will be asked if they are interested in participating and agree to voluntarily complete the screening procedure. Participants will electronically indicate their agreement and then take the survey. The study will use SSL encryption for transfers of information online and data will be stored in the secure, HIPAA-compliant servers of SurveyGizmo. The Emory AC team maintains a business partner HIPAA agreement with SurveyGizmo.

For those who meet eligibility criteria, the survey will ask for the first name, e-mail, and phone number of the participant. Potential participants who do not meet eligibility criteria but are residents of a recruiting city and are at least 15 years of age will be asked if they would like to be contacted about other research studies and, if so, to provide contact information. Participants under 15 years of age are not asked to provide contact information.

The Analytic Core will securely share the contact information of eligible participants with SRV sites via a secure iTech Box account. SRV staff will enter the eligible participant into SMART (described in more detail later in the protocol) for scheduling and contact participants to schedule an in-person visit at the SRV. SRVs will also have the option to have the participant complete the online screener the day of the in-person visit; study staff can view eligibility on the browser window once the screener is complete or review the automatic eligibility email sent after survey completion.

5.0 STUDY PROCEDURES

5.1 Enrollment

Individuals who are eligible will be contacted and scheduled for an in-person visit to the SRV at the participant's earliest convenience. SRVs will also have the option to have the participant complete the online screener the day of the visit. During the visit, the eligibility of the participant will be confirmed, details of the study will be explained and informed consent/assent obtained.

Individuals who do not consent or assent to participate will be asked if they are willing to provide their reason for declining participation; responses will be recorded on a CRF. Individuals assessed as ineligible for enrollment will have the reason(s) for ineligibility recorded.

The study team may request tabulated information on individuals who participated in the enrollment process, but did not provide informed consent/assent and the reasons these individuals refused to participate. These data will provide general information on the population that is recruited at the SRVs into the study.

After informed consent/assent is obtained, the participant will complete a CASI baseline assessment. For Aim 3, randomization will only occur AFTER a baseline assessment is completed.

In Aim 3, participants assigned to the intervention group will be considered enrolled in the study after they have completed the baseline assessment, been randomized, and completed app onboarding (for the intervention arm). Participants assigned to the control arm will be considered enrolled in the study after they have completed the baseline assessment, been randomized, and been given standard of care materials.

CRFs will be completed by study staff to capture the participant's eligibility and enrollment.

5.2 Locator/Contact Information

Once the participant is consented/assented, designated site study staff will complete a Locator/Contact Information Worksheet with the participant and/or enter the participant's contact information directly into SMART Web during the enrollment visit. Participants will be asked to provide a working phone number and/or valid email address through which they can be reached. Participants will also be asked to provide social media contact information, if the participant is willing. In addition, participants will be asked to provide valid contact information for two family members and/or friends who can be called in the event the participant cannot be reached by phone or email. Participants will be asked if messages can be left at the numbers provided. Study staff will not leave messages unless expressly permitted to do so by the participant which also will be documented on this form. If permission is given to leave messages, site study staff will assure participants that messages left with a family member or friend will only ask the participant to contact study staff and will not include any protected health information or information related to study participation.

The Contact Information Worksheet will not contain any study data and will be maintained under double locks at the study site, separate from all study records, with access limited to designated site research personnel.

5.3 Randomization Procedures

Aim 1 (focus group theater testing) and 2 (open pilot) will not include random assignment.

Aim 3 Pilot Randomized Controlled Trial:
Only participants who express willingness to download the "MyChoices" app for HIV prevention, meet eligibility criteria, provide informed consent/assent, and complete a baseline assessment will be eligible for randomization. Randomization will occur at a 2:1 ratio with 40 YMSM randomized to the experimental condition (~10 to 20 at each site) and 20 randomized to the control condition (~5 to 10 at each site). Randomization will be stratified by site and age (15-18, 19-24).

This allocation will allow us to efficiently gather additional data on app utilization. Randomization will be based on a pre-generated list created by the Analytic Core, with random blocks of size three or six. After consent/assent and completion of the survey assessment, the study coordinator will assess whether the participant is randomized to receive the Intervention or Control condition. **"MyChoices" Intervention Condition:** Individuals who receive "MyChoices" will be given brief instructions on the purpose of the app, how to access it, and an overview of how to use it. Participants will be encouraged to explore all components of the app and use it routinely. **Standard of Care Condition:** Following screening, participants in both conditions will receive standard of care prevention material consisting of online provision of information regarding recommendations for HIV testing and referrals to local HIV testing sites and prevention services.

5.4 Intervention/Investigation Procedures

Following an iterative process of app development, "MyChoices" will be further refined through theater testing with focus groups (Aim 1) and an open technical pilot (Aim 2) at iTech SRV sites. To plan for an R01 efficacy trial proposed within the current iTech project, we will conduct a pilot RCT (Aim 3) to assess acceptability, feasibility, and preliminary efficacy of MyChoices.

5.4.1 Aim 1: Theater Testing Focus Groups

To refine the "MyChoices" app and enhance components designed to increase PrEP uptake among YMSM, study staff at each SRV will conduct theater testing of the app. In these groups, we will demonstrate the mobile app to participants and elicit feedback on the following topics: overall feedback on the interface, appeal, and usability; ways to maximize acceptability; components that they like and/or dislike; and areas for improvement (e.g., strategies for condom promotion). Moreover, in order to enhance components aimed to increase PrEP uptake and guided by the SCT model, we will elicit input from participants in the following areas: 1) potential content to address PrEP-related self-regulation may include recommendations to speak with a provider about PrEP if their risk assessment indicates potential eligibility, and how their risk may

be impacted if they take PrEP; 2) content and functionalities to improve PrEP use self-efficacy including videos showing couples discussing PrEP, GPS-enabled provision of links to local PrEP providers which allows them to manage their own PrEP care, and guidance on questions to ask providers about PrEP (e.g., dosing, side effects, necessary follow-up); 3) potential content to address environmental influences on PrEP uptake, including information on insurance and other payment options for PrEP. Additionally, to prepare for the pilot RCT, we will ask participants about their attitudes regarding documenting their testing practices and results through signed medical releases and sending photos of test results to document completed testing. Theater testing groups will last 60-90 minutes, and discussions will be audio recorded and transcribed verbatim by the AC.

5.4.2 Aims 2 and 3: MyChoices Intervention

For all participants enrolled in the Aim 2 open technical pilot and for participants randomized to the intervention arm of the Aim 3 pilot RCT, study staff will assist participants in downloading the app, provide instruction on its use, and will be available to explain the relevant app features or set up customizable features (e.g., reminders for HIV testing). Participants will also be encouraged to explore and use other components of the app.

"MyChoices" was guided by the SCT model and includes three major functions that are designed to promote self-efficacy, self-regulation, goal-setting, and environmental influences in order to impact behavior change (see Table below). Tracking and Self-Monitoring HIV Risk: In order to target self-regulation, brief surveys within the app are used to assess behavioral patterns of YMSM, particularly around sexual relationships, which are then used to help customize the app for each user. For example, users who report having a main partner will be informed about couples counseling, or users who report difficulties using condoms will be provided information about PrEP and provided links to HIV prevention services at local sites. Users are also able to enter HIV and STI test results to keep track of past test dates and results. HIV and STI Prevention Information: In order to improve self-efficacy for HIV testing and HIV prevention overall, quizzes and infographics that appeal to YMSM have been incorporated into the app, focusing on promotion of HIV prevention and regular HIV testing. Infographics are interactive to allow users to obtain more detailed information on topics that are most relevant to them, thus personalizing the app experience. Links to videos of YMSM discussing the following are included: approaches that YMSM can use to prevent HIV transmission (including condoms, treatment as prevention, and PrEP); reasons for routine HIV testing; and the importance of engaging in care if one tests positive, or initiating PrEP if one tests negative and anticipates engaging in condomless anal sex. The app also allows users to order OraQuick HIV home testing kits and STI home collection kits referred to as CareKits (for gonorrhea and Chlamydia and syphilis), and to explore different types of condoms and lubricants to learn more about them, as well as to create customized packages of these items to be shipped to them or to a local site where they are comfortable picking up a package. Test kits and condom packages will be provided as a service through the iTech Technology Core and will be packaged specifically for this project. STI home collection CareKits will include a pre-paid mailer to be returned to Kraft Laboratory at Emory University for testing. These kits have been used in an ongoing RCT of "Keep It Up", for which U19 co-PI, Dr. Patrick Sullivan is the Atlanta site PI, and they have been acceptable to the young (18-29 year old) men in that study. The study will follow the STI and HIV CareKit, Condom and Lubricant Ordering Standard Operating Procedures developed by the CareKit team at Emory. Additionally, the app includes information on testing sites and local PrEP clinics (e.g., telephone, address, hours of

testing, etc.), and external links to specific site web pages that are near the user (determined using GPS technology). HIV Testing Plan: Acknowledging the central role of goal setting and environmental influences on health behavior, the app allows users to create an HIV testing plan by allowing them to compare and choose different screening options (e.g., home self-testing, antigen, rapid). Questions about HIV transmission behaviors and testing history are then asked to create a tailored testing plan. After an HIV testing plan is developed, users have the option to customize reminders for the timeframe selected (e.g., user is pinged every 3 months as a reminder to get tested). Users are able to select from a list of phrases or create their own to ensure privacy. Moreover, geofencing technology allows users to be notified when in the vicinity of testing locations, based on the GPS location, during the testing timeframe.

Social Cognitive Theory constructs, associated "MyChoices" components and intervention measures

SCT Constructs	App Components	Measures
Self-regulation	Self-monitoring through: risk assessments; HIV testing plan; HIV/STI results tracking; STI symptoms checklist	Frequency of use of relevant app components; perceived HIV/STI risk
Self-efficacy	Infographics and videos showing youth talking about HIV testing; GPS-enabled links to local HIV testing clinics; ordering of home-based testing kits, condoms, etc.	HIV testing self-efficacy; PrEP use self-efficacy; condom use self-efficacy
Goal-setting	HIV testing plan with goal setting for testing frequency	Frequency of use of HIV testing plan
Environmental influences	Customized reminders for HIV testing based on testing plan, including use of geofencing technology	Frequency of use of reminders; frequency of testing due to geofencing technology

Standard of Care Comparison Condition. Following screening, participants in both conditions will receive standard of care prevention materials. These will consist of online provision of information regarding recommendations for HIV testing and referrals to local HIV testing sites and prevention services, along with an informational brochure about PrEP.

5.4.3 Research Staff Training

All proposed study staff have participated in the required trainings in participation and conduct of studies that involve human subjects, and any future study staff will do so upon hiring. Training for all staff includes (but is not limited to) an overview of the study, study procedures and human subjects issues (informed consent process, confidentiality), methods for establishing comfort with the sensitive issues, including discussion of sexual behaviors, that will likely arise in the course of the focus groups or assessments, review of the study instruments, their required elements and the inherent flexibility built into them Human Subjects Protection for Social and Behavioral Research, Good Clinical Practice, informed consent, quality management, confidentiality, and reporting of adverse events.

For Aim 1 focus groups, the PI team at Fenway Health will train study staff at the SRV locations to facilitate the focus group discussions.

5.4.4 Medical Record Abstraction

The goal of the medical record abstraction is to explore whether it is feasible to collect more objective measures of HIV and STI testing and PrEP uptake, and to compare the medical records to self-reported data on these measures. Medical record abstraction will occur following the completion of the final follow-up assessment and will cover the entire study period. This abstraction will only occur if the participant has signed a medical records release form for the institution where records are being requested from. Signing a medical record release is not a requirement of enrollment—participants may refuse without being withdrawn from the study. Only records verifying HIV and STI testing information, and records related to PrEP initiation will be requested. The period of abstraction will begin at the baseline visit and end up to 12 weeks following the 6 month follow-up assessment in order to accurately capture any PrEP initiation activity following mobile app use. Standard study CRFs with study ID will be completed using the medical records, and all medical records will be immediately de-identified (black out any identifiers) and labeled with study ID.

5.4.5 Intervention Monitoring/Quality Control

Given that the intervention is in the form of a mobile app, there will not be interventionists providing content. A study checklist will be used to ensure that the research staff member assists participants in downloading the app, provides instruction on its use, and explains the relevant app features and sets up customizable features (e.g., reminders for HIV testing).

App analytics, including logins to the app and use of different app components, will be monitored for the technical pilot and pilot RCT aims of this project. Any issues that are detected will be discussed with the protocol team and site research staff, and a remediation plan will be developed and implemented at the sites.

6.0 EVALUATIONS AND MEASURES

The screening assessment must be performed within 30 days before study enrollment.

All evaluations and measures will be reviewed and approved by the UNC-CH IRB prior to use with human subjects. Below is a summary of the measures for each aim of the study.

6.1 Aim 1: Focus groups

6.1.1 Pre-entry or screening evaluations/measures (at -30 – 0 days prior to enrollment)

- Age (15 to 24 years)
- Sex (assigned male sex at birth)
- Current gender identity (male)

- HIV status (self-report being HIV uninfected or HIV status-unknown)
- HIV testing history
- PrEP use history
- Reports at least one episode of anal intercourse with a male partner during the last 6 months
- Own or lease an Apple (iOS) or Android mobile phone

6.1.2 Quantitative assessment (at enrollment visit)

- Demographics
  - Age, sex, gender identity, race/ethnicity, education
- Health
  - STD testing history and diagnoses, HIV testing history, PrEP use history
- Sexual Risk Behavior
  - Number of partners, condom use
- Technology use
  - Use of internet and mobile apps, accessing health information, meeting sexual partners, interests in health apps

6.1.3 Focus group guide (at enrollment visit)

- Overall feedback on the interface, appeal, and usability;
- Ways to maximize acceptability;
- Components that they like and/or dislike, and areas for improvement
- Feedback on specific content and functionalities guided by SCT model, including self-regulation, self-efficacy, and environmental influences
- Feedback on HIV/STI self-testing collection kits and instructions
- Attitudes regarding documenting their testing practices and results through signed medical releases and sending photos of test results to document completed testing

6.2 Aims 2 and 3: Open technical pilot and pilot RCT

6.2.1 Pre-entry or screening evaluations/measures (at -30 – 0 days prior to enrollment)

- Age (15 to 24 years)
- Sex (assigned male sex at birth)
- Current gender identity (male)
- HIV status (self-report being HIV uninfected or HIV status-unknown)
- HIV testing history (self-report having not had an HIV test in the past 3 months)
- PrEP use history (self-report not currently taking PrEP)
  - Participants ages 15-18: self-report at least one episode of anal intercourse with a male or transfemale partner during the last 6 months
  - Participants ages 19-24: self-report evidence of high risk for acquiring HIV infection including at least one of the following:

        - at least one episode of condomless anal intercourse with an HIV-infected or unknown HIV status male or transfemale partner during the last 6 months
        - anal intercourse with 2 or more male or transfemale sex partners during the last 6 months
        - exchange of money, gifts, shelter, or drugs for anal sex with a male or transfemale partner during the last 6 months;
        - sex with a male or transfemale partner and has had an STI during the last 6 months
- Able to understand, read, and speak English
- Owns or leases a phone with Android platform (for Aims 2 and 3) or iOS platform (Aim 3 only) and has an active data plan

6.2.2 Pre-intervention (baseline) evaluations/measures (at enrollment visit)

- HIV Testing: participants will be asked to self-report on frequency of HIV testing
- PrEP care linkage: participants will self-report whether, in the past 3 months, they made and attended a clinic appointment for PrEP initiation, whether they were prescribed PrEP, and whether they utilized PrEP
- Additional behavioral measures
    - Sexual risk behaviors: we will use the AIDS-Risk Behavior Assessment (ARBA), a computerized self-interview designed to assess self-reported sexual behaviors.
    - Substance use: To assess risky substance use, we will use the ASSIST screening tool – an 8-item validated questionnaire developed by the World Health Organization and addiction researchers. We will also ask the degree to which they use each substance during sex.
        - Access to and utilization of health care: we will assess whether participants see a medical provider regularly, whether they received testing for STIs, other than HIV, and if they were treated.
    - SCT model constructs
        - Self-regulation: perceived HIV and STI risk, and STI symptom knowledge
        - Self-efficacy: HIV testing, PrEP use, and condom use self-efficacy
        - Environmental influences: perceived utility of reminders for HIV testing
        - Potential moderators of the intervention
            - Demographics: Age, student status, education level, income, living situation, employment, insurance status, depressive symptoms, anxiety, trauma, and abuse

6.2.3 On study evaluations/measures

- Biological endpoints via home test kits
    - HIV infection: this proposal will utilize the OraQuick® ADVANCE™ [sensitivity: 99.6% (98.5–99.9); specificity: 100% (99.7–100)], an HIV rapid test that is FDA-approved for HIV-1 and HIV-2 testing for at-home testing (intervention arm).
    - Participants in the intervention arm will be asked to self-report STI and HIV testing results into the MyChoices app.
    - Additionally, we will also request all participants (control and intervention arms) to sign

medical release forms for the release of their official testing results from the respective testing site so that study staff can collect official results.

6.2.4 Follow-up assessments (2-month post-baseline for open pilot and 3- and 6-month post-baseline for pilot RCT; study window: ± 4 weeks)

All of the same measures assessed at baseline as well as the following additional measures:

- Acceptability
  - System Usability Scale (SUS): a validated 10-measure scale that assesses subjective usability of a system, or, in this case, an app. It is scored from 0 to 100, and a score of 50 or greater indicates that the app is acceptable.
- Feasibility
  - We will use app analytics to determine whether at least 60% of individuals randomized to the intervention condition opened the "My Choices" app at least one time after their initial introduction to the app by research staff.
  - Proportion of participants who complete their HIV testing plan
- HIV Testing: participants will be asked to self-report on frequency of HIV testing since last assessment. The primary HIV testing measure will be the proportion of participants who self-report at least one test during the follow up period. We will also explore the concordance of self-report with data collected by medical release and using data electronically self-reported in the app, including home testing kits provided by request through the app.
- App-Specific Measures
  - Frequency and duration of app use
  - Pages and functionalities most and least utilized
  - Responses to each question within the assessment, quiz, screening, and test results reporting
  - Information about each test plan event: location, date(s), type selected, frequency
  - Which testing locations were viewed, and whether they were accessed using the map or the list view.
  - Reminder settings and preferences
  - Number of HIV testing kits, STI home testing CareKits, condoms, and lube requested

6.2.5 Exit interview guide (0-30 days following: final assessment for Aim 2, three months post enrollment for Aim 3)

- acceptability and utility of the app
- feedback on how the app and intervention components could be strengthened
- identify areas of the app needing improvement for future iterations
- feedback on study procedures
- acceptability of the assessments with respect to duration and relevance
- seroconversion and app use, linkage to care

7.0 DATA COLLECTION AND SITE MONITORING

7.1 Development of Protocol and Case Report Forms

The Management Core, in collaboration with the Protocol Team, is responsible for the development of this protocol as well as the Case Report Forms (CRFs)) needed to collect the information required to implement this protocol.

7.2 Data Records

Participant-related study information will be identified through a study ID number (SID) and participant code comprised of the first letter of the participant's first name and two-digit day of birth on all participant CRFs, audio files, transcripts, and Computer-Assisted Self Interview (CASI) files. All study-related information will be kept in double-locked, limited access areas at each study site. Participant names and their SID and initials will be stored separate from other study information in SMART, accessible only to designated study staff, iTech site monitors, and representatives from the NICHD. SIDs will not be entered into the mobile app and instead a unique app ID will be assigned to each participant and used when logging into the app. These unique App IDs are assigned via the Study App ID log and connected to the app via back-end web access by study staff. Original source documents for individual participants will be maintained at the respective SRV site and will be accessible only to the study staff. Data from original source documents will be transcribed on CRFs as applicable.

7.3 Data Collection

7.3.1 CRFs

Study monitoring data, including information about eligibility, demographic data, and monitoring untoward effects, will be collected on CRFs. All CRFs for this study will be available for download from a secure iTech Box account.

7.3.2 Study assessments

Self-administered assessments at baseline and at follow-up visits (for the open pilot and pilot RCT) will be completed by participants on study computers (for baseline) and personal devices (for follow-up assessments, though participants will also be given the option to return to the SRV to complete the follow-assessment on study computers) via online Computer assisted self-interview (CASI) surveys hosted on SurveyGizmo.com. We use SSL encryption for transfers of information online and data will be stored in the secure, HIPAA-compliant servers of SurveyGizmo. The Emory AC team maintains a business partner HIPPA agreement with SurveyGizmo.

7.3.3 CASI Data Security

Only authorized users with a login name and password will be able to access and open the assessment through the internet site. To ensure data privacy, as data are entered in real time, it will be encrypted during transmission to the SurveyGizmo server, and that data will be regularly downloaded by AC staff and stored in a secure database within the AC data center at Emory University.

7.3.4 VSee Platform Description

For the online qualitative interviews being conducted in the Aim 2 open technical pilot and Aim 3 RCT, the study staff interviewers will rely on VSee platform. When using VSee, participants will have the option to use VSee in several formats: face-to-face video chat, video chat in which they can see the interviewer but the interviewer cannot see them, audio chat only, or a text-based conversation. VSee is compatible on PCs, tablets and smartphones. Unlike other video-chat platforms (e.g. Skype), VSee is HIPAA-compliant. VSee includes the following functions to protect users:

*End-to-end encryption without a man-in-the-middle listener***.** In WebEx, Vidyo, Tandberg, and Polycom architectures, media is sent to a server (also called a video relay or MCU). Although encryption is applied from the user's computer to these servers, the servers still have full access to the user's media. In contrast, VSee uses end-to-end encryption where no server, including VSee servers, has the decryption key. VSee uses public/private RSA keys to exchange a 256-bit AES session key with the property that only the endpoints have the AES session key. VSee uses FIPS 140-2 certified 256-bit AES encryption.

*One port***.** VSee uses a single port for call signaling and media. The VSee protocol is structured so that only the outgoing port needs to be open because return traffic is always structured as responses to outgoing traffic. This allows administrators to set a policy where if users inside their network are using VSee, then their firewall lets VSee traffic securely cross the firewall; however, if users inside their firewall stop using VSee, then the firewall will block external port scans.

*Automatic HTTP/SSL tunneling***.** VSee prefers to use UDP since it allows higher performance video. However, if the firewall does not allow UDP, VSee will automatically switch to HTTP/SSL tunneling.

*Cloud Control***.** VSee's cloud solution allows enterprises to maintain central control of their security policies to a large number of end points even though the service is hosted by VSee. It does this by having VSee clients always connect first to VSee servers in the cloud, where the policies are controlled. The cloud servers determine whether any of these security policies should be applied and enforces them at the VSee client. This allows us to set our own security settings and to record the sessions.

*No-install client***.** Video conferencing software clients tend to be large and to leave a big footprint on the user's system. Almost all of them require administrator permissions to install. Once the client software gains administrator permissions, they can severely compromise computer

security. VSee is a lightweight client that does not require administrator permissions or installation.

VSee offers the HIPAA-required Business Associate Agreement (BAA) where VSee agrees to be responsible for keeping all patient information secure and to immediately report any breach of personal health information. In this study, the iTech Technology Core will enter into a BAA with VSee, and this will be extended to cover the proposed activities. The VSee sessions will include identifying information (e.g., images of the participant, voice recordings). All identifying information will be stripped from the recorded VSee sessions before they are sent to the analysis team for content analysis.

7.4 Data Submission

7.4.1 CRFs

Although the iTech projects will involve substantial online follow-up, this protocol will also use CRFs to collect data on key study visit data (e.g., enrollment and randomization assignment), study milestones such as completion or discontinuation, results from medical records, study laboratory results, and adverse events (AE). AC staff will work with study investigators and the MC to develop and design the CRFs. During study conduct, the SRVs will maintain the CRFs in secured locations, and transmit CRF data to the AC using DataFax, a leading multi-site database environment for HIV RCT. DataFax can receive and transcribe CRF data via fax and scan, or allow for direct data entry. It provides for monitoring form completion and data quality, and a system for data querying and resolution with SRVs, while maintaining an audit trail. The AC uses DataFax for MSM studies and RCT and maintains a DataFax Linux server at Emory.

7.4.2 Audio Data

All focus groups and individual qualitative interviews will be audio recorded and audio recordings will be transcribed verbatim by a professional transcription service through the AC. Audio files will be erased after being transcribed and transcripts will be de-identified.

All audio files will be kept confidential and stored in a locked/limited access folder on secured servers, which is only accessible to designated study staff. All members of the research team will be trained in confidentiality and have signed confidentiality agreements. A professional transcription service, experienced in the handling of confidential data, will be used to fully transcribe verbatim all audio files. Prior to receipt of the first audio file, the transcription service will be instructed to exclude from the typed transcript identifying information (e.g., a name) that may have been verbalized during the course of the focus groups.

7.4.3 CASI Data Transmission

Only authorized users with a login name and password will be able to access and open the survey through the internet site. To ensure data privacy, as data are entered in real time, it will be encrypted during transmission to the SurveyGizmo server, and that data will be regularly

downloaded by AC staff and stored in a secure database within the AC data center at Emory University.

7.4.4 Retention data

The study will use a HIPAA-compliant web-based platform entitled Study Management and Retention Toolkit (SMART), which is a SaaS (Software as a Service) based mobile application aiding studies with various aspects of participant recruitment, study implementation, and retention. The application has the ability to securely manage participant information across multiple studies and customers simultaneously, stratifying participant information by study and site. SMART includes an admin web portal and a participant facing mobile app (optional), which allows for secure messaging, study calendar management, self-scheduling by participants, secure photo uploads, and longitudinal tracking of participants from screening to study completion. The ability to designate specific roles to all SMART users allows for greater control around permissions and accessibility to participant information. Users can even be limited to a reporting only role, which allows for study oversight through real time aggregate reporting, but no access to PHI. SMART is a licensed service of the Center for AIDS Research (CFAR) at Emory University, Prevention Science Core. Utilization of the mobile app is optional and the admin web portal will fully function without it.

The following information outlines the security of the three SMART components: (1) the admin web portal, (2) the participant mobile app, and (3) a web service that acts as a liaison between the mobile app and the study database.

Admin Web Portal. The admin web portal is a web-based application developed using Microsoft .NET technologies. It uses SQL server as backend database. The application requires two servers to host: (1) Web server [Windows server with IIS] and (2) SQL server [Standard or Enterprise version]. Both these servers are to be placed behind a firewall. Web server will have a public IP to access the server using VPN. SSL certificate is to be installed on the web server. The admin website will be rendered over SSL (https).

The application uses form authentication (no integrated authentication such as AD). All passwords are stored encrypted within the database. System will also be using database level encryption, which will prevent any copying of information from one database to another. Web application also uses an automatic logout feature after a certain period of inactivity. By default, the inactivity duration is set to three minutes.

Study staff can only first gain access to the admin web portal if granted by a study or site administrator. Their assigned user role will determine their permissions to perform different actions and even view PHI. Email notifications are sent from the system (without the need to login) when: (1) a staff member requests to reset their password, (2) role assignments to a study are made, (3) an event/visit staff are scheduled to work is nearing, (4) a new task is assigned to a staff member, or (5) they are designated as a staff member to receive alerts of positive test results. All participant communications are performed using secure messaging through the message center (inbox) implementation within the mobile app. If the mobile app is not utilized by a study, communications are sent as standard email or text messages to participants.

Mobile App. The mobile app, developed natively for iOS and Android platforms and available for free in the App Store and Google Play Store, is an optional feature the study can utilize for self-scheduling, communication, photo uploads, and updating contact information. The study will indicate during the initial setup within the admin web portal whether the participant mobile app is utilized or not. If the app is utilized, participants will receive download instructions after their information is entered into the admin web portal. Only participants listed in an active study who validate their email or phone number against the contact information listed in the admin web portal will be able to proceed into the app. For validation, the app uses both traditional form authentication as well as social login (Facebook and Google). The social login feature will only work if the email associated with either social account matches the contact information within the admin web portal. The app does not request anything other than basic information from these authentication services. Participants cannot "remember" their password on the mobile device for automatic logins to ensure privacy. All participant data and activity status is maintained within a secure and encrypted SQL Server database. To create the connection between the admin web portal and the mobile app, each participant is assigned a unique ID within the application, which is associated with their login credentials. When a participant has been successfully authenticated through the mobile app, the admin web portal will send their specific information to their phone through the established secure session (web APIs using SSL). The app will not store the information presented locally on the phone. Local data storage is used only for storing some minimal non-PHI information, such as app settings. The mobile app implements an automatic logout when there is inactivity for more than three minutes. If a participant should need to re-download the app on a new device, login and password authentication will be required again.
The mobile app has push notifications that are primarily used for reminders and notifications of new messages. Push notifications displayed on the participant's phone will be generic in nature and not contain any PHI. Reminders and notifications within the mobile app inbox will also be generic in nature, with any message containing sensitive information requiring a pin, established during registration as a secondary authentication, to open within the mobile app. Firebase cloud messaging service is used as a communication channel for these notifications. No PHI is passed through Firebase. Push notifications are customizable in the study setup, and samples of system notifications include: "You have a new message in your inbox," "You have an upcoming event for March 7, 2018," and "You have a pending task."

Web Service. A web service will also be hosted on the web server. This service is used by the mobile application to retrieve and store data. The service will utilize secure socket layer (SSL) for communication.

7.4.5 Mobile application data

MyChoices follows best practices for collecting, storing, and transmitting data. The application will be available to users in Android (and iOS for Aim 3 only) as a native app. Users initially access the app by entering their email address and a registration key (supplied following completion of the eligibility survey), and setting up a user-generated password. On subsequent visits to the app, users must supply their username and password, or may choose to create a PIN through their device settings. If the app is removed from a user's device, all associated data is removed from the device. In this case, user data is not deleted from the developer database. To capture data analytics as described above (see Data Collection), user app activity is sent to a web-based

administration portal (Admin Portal). The Admin Portal is a Microsoft SQL Server and .NET application hosted in a FedRAMP compliant hosting environment. The Admin Portal is secured via SSL encryption and each user requires a unique username and password for access. Only study staff at the coordinating site and staff at the analytic core will have access to this data. Within the Admin Portal, de-identified data on app usage is stored. SIDs will not be entered into the mobile app and instead a unique app ID will be assigned to each participant and used when logging into the app. These unique App IDs will be provided by the developer. Only designated study staff will be able to link the unique app ID to the SID. If the app data were accessed independently without the SID link, no participant information would be identifiable. No personal information is stored in the Admin Portal at this time, other than the user's email address.

7.5 Data Quality Assurance

Investigators receiving federal funding must adhere to the Code of Federal Regulations (CFR) to protect research participants and produce reliable study information. Sites participating in research sponsored by the NICHD need to have an internal quality assurance (QA) plan that will identify problems and correct errors in research study records.

7.6 Role of Data Management

The MC will provide instructions concerning the recording of study data on the CRFs, and entry of the data into RDC *(and CASI/CAPI administration and transmission if applicable)*.

7.7 Study Site Monitoring and Record Availability

Site monitors from the MC will visit participating study sites to review a selected portion of the individual participant records, including assent/consent forms, CRFs and supporting source documentation to ensure the protection of study subjects, compliance with the protocol, and accuracy and completeness of records. Regulatory files, as required, will also be inspected to ensure that regulatory requirements are being followed.

The site investigator will make study documents (e.g., assent/consent forms, case report forms) *and pertinent hospital or clinic records* readily available for inspection by the local IRB, the UNC-CH IRB as the single IRB (IRB of Record), the site monitors, the NICHD, the Office of Human Research Protection (OHRP), or the sponsor's designee for confirmation of the study data.

8.0 PARTICIPANT MANAGEMENT

8.1 Tracking Participants / Follow-up

Study staff will verify participant contact information at baseline and update this information if needed at time of follow-up.

Study staff will contact participants prior to their target date to complete follow-up study procedures. Study staff will use both a preferred and, if necessary for youth who are difficult to

reach, backup method of contact as indicated at baseline (e.g. mail, alternate phone numbers, e-mail, text message, social media contact information), to contact participants to complete follow up study procedures. Additional reminders will be provided on/after the target date as needed to ensure completion of study visit procedures. Subjects will be asked whether or not messages can be left for each of the phone numbers that they provide. They will be informed that messages will not contain any information regarding the nature of the project.

8.2 Compensation

The decisions around compensation will be determined separately by each SRV, listed in the SRV's informed consent/assent form, and approved by the single IRB (the UNC-CH IRB).

The web-based CASI survey and online exit/in-depth interview will be conducted online, however participants will be able to come into the SRV to complete these procedures if preferred on SRV computers or tablets. Site study staff will be notified when a subject has completed a CASI survey and online exit/in-depth interview on his own and the compensation will be provided to the participant. Compensation can be provided in person, or sent to participants electronically or via mail, if allowed at the SRV.

8.3 Intervening on "Social Harms"

Some of the questions in the quantitative assessments are related to potentially sensitive topics including intimate relationships, drug use, and sexual behaviors. Social, psychological, and interpersonal harms may include being discriminated, feeling stigmatized, emotional distress, as well as feelings of discomfort and embarrassment. Additionally, this study involves provision of home HIV/STI testing which may cause participants to worry or become anxious. If the HIV/STI test results are reactive (e.g., a "preliminary positive" on the HIV rapid antibody test), participants may become depressed or feel anxious.

All study sites have specific policies governing the treatment of human subjects. These policies specify that medical and psychological assistance will be available in the immediate environment in the event a participant should experience any adverse reactions resulting from study procedures.

While participants will be informed that they may refuse to answer any question at any time, responses or reactions to certain questions may indicate distress on the part of the participants. Participants experiencing mild distress during a study visit will be offered a small break or to reschedule the interview at later date. In the unlikely event that a participant experiences considerable distress, they will be offered a voluntary clinical assessment and/or counseling on site. As a result of participant self-report, study staff discovery, or routine study assessment, the study staff may become aware of a social harm. Study staff will be trained to make appropriate referrals for clinical care in consultation with the PIs or designee to help participants cope with any feelings and/or questions they have which may arise. All information disclosed to the researcher will remain confidential if the participant chooses not to complete the study.

If at any time during the study, a participant divulges that he or she is at risk for harm, including but not limited to being abused or experiencing violence, if harm is suspected or likely, or if the participant states he or she is suicidal/homicidal, measures will be taken to ensure his or her safety. Reporting will be done as appropriate to the situation and the legal statutes, including reporting to child protection agencies or other appropriate agencies, and referrals will be provided to appropriate support, counseling, or treatment resources.

8.4 Criteria for Premature Study Discontinuation

The principal investigator has the authority to withdraw any participant at any time if it their opinion it would be in the best interest of the participant. The participant will be informed of this withdrawal and explained the rationale. Withdrawal will be documented in the study tracking system.

Subjects will be prematurely discontinued from the study if any of the following occurs:

a. The subject withdraws consent/assent;
b. The participant is unwilling or unable to comply with study procedures;
c. The investigator believes that ongoing participation may cause harm to the participant or study staff;
d. The investigator believes that ongoing participation may impact the integrity of the study data;
e. The study is cancelled by the *NIH (or iTech, or other administrative entity)*;
f. The study is cancelled for other administrative reasons; or
g. Death of the subject.

Participants may end their participation in the study at any time. Participants who are prematurely discontinued from the study may be allowed to re-enroll into the study on a case-by-case basis. No further data collection will occur from the date the decision is made to permanently discontinue the subject from the study. Participants who experience distress during the study while in the SRV clinic will be offered counseling on site. Participants who experience distress during the study and do not come to the SRV clinic for a visit will be provided a list of community referrals via phone or e-mail. Any unexpected adverse events that meet the New Safety Information (NSI) reporting criteria will be immediately reported to the UNC-CH IRB and the respective sites' IRBs if applicable. The *Study Stop Form* will be completed at this time.

Participants who seroconvert during the study will not be discontinued from the study and will continue to have access to the app and its functions.

9.0 MONITORING UNTOWARD EFFECTS ASSOCIATED WITH OR RESULTING FROM STUDY

Site study staff must first follow their own IRB's procedure for reporting and managing untoward effects.

There are two types of untoward effects to be identified: (1) those related to the participant, and (2) those related to the study staff.

1. The study will catalogue any untoward effect related to the participant. Reporting is required for occurrences including social harms, psychological distress, and serious life-

threatening events such as suicide attempts. These may be immediately apparent to the study staff, such as the participant's emotional upset requiring referral for counseling; or they may be delayed and reported later to study staff, such as physical harm to an individual for having participated in the study.

Study staff will notify the iTech team of any untoward effects using the iTech QNS accessible through the iTech website (www.itechnetwork.org) within 24 hours of becoming aware of these untoward effects. Study staff will be briefed during the training on the scope of possible untoward effects and instructed to report events.

In addition to social or emotional harm, this study will collect, manage, and report on adverse events related to home HIV and STI testing kits ordered through the MyChoices app. It is anticipated that adverse events will be reported to study staff by phone or during study visits. Study staff will record adverse events on an adverse event CRF. Unanticipated Adverse Events (UAE) associated with these kits will be reported to the study site's IRB as applicable. In this case, a UAE is any AE that the investigator determines to be attributable to the HIV or STI home testing event that is serious or not previously identified in nature, severity, or degree of incidence in the product's labeling. The determination of a UAE will be made by the Principal Investigator at the SRVs.

i. A positive HIV or STI result, as determined by the FDA-approved testing, will not be documented as an AE, as HIV results are part of the endpoint evaluation of the study.
ii. The study will follow the UNC-CH IRB policy and each SRV's IRB policy for the reporting of Serious Adverse Events (SAE). The Principal Investigator at the SRVs will determine seriousness, relationship to study participation, and severity. An adverse event is serious if it:
    1. Is fatal or life-threatening
    2. Requires or prolongs hospitalization.
    3. Results in persistent or significant disability/incapacity
    4. Is a congenital anomaly/birth defect, or is medically significant, may jeopardize the subject, and may require medical or surgical intervention to prevent one of the outcomes listed above.

2. Study staff may encounter untoward events during sessions that personally affect them. Training and guidance will seek to minimize this risk. Nonetheless, an assessment of the cost of conducting this study must include cataloguing these events as well. The protocol chairs should be notified of these events so that they may be immediately addressed, evaluated, and guidance modified or expanded to minimize similar risk to other study staff.

10.0 STATISTICAL/ANALYTIC CONSIDERATIONS

10.1 Introduction

Qualitative and quantitative data analysis will be supported by the iTech Analytic Core.

10.2 Power Estimates

10.2.1 Aim 1: Theater Testing Focus Group Discussions

For qualitative data collection, sample size is driven by thematic saturation. While this can occur with as few as 6-12 people (Guest 2006), it is typical to include approximately 20-40 in qualitative health research.

10.2.2 Aim 2: Open technical pilot

We judge that 12-15 participants would be enough to trial all intervention procedures and obtain feedback on study procedures and documents.

10.2.3 Aim 3: RCT pilot

As a pilot study, the primary emphasis is on establishing acceptability and feasibility of "MyChoices." Power to find group differences in the efficacy outcomes is limited; to find statistical significance, the effect sizes would need to be large. With a two-tailed p-value of 0.05, 60 randomized at a 2:1 ratio and with 20% attrition there will be 80% power to detect a 50% difference across the two conditions. The large minimum detectable effect size, typical of pilot studies, will require careful interpretation in light of overall patterns.

10.3 Statistical Analysis Plan

10.3.1 Aim 1: Theater Testing Focus Group Discussions.

A rapid analysis of the data from the theater testing will be conducted by the PI team at Fenway Health using detailed notes taken during the focus group discussion. Additionally, the iTech Analytic Core will assist with more in-depth coding of the data from the theater testing. A codebook of a priori and emergent themes, including operational definitions of all codes and sample quotations to illustrate how to apply each code, will be created. Two study team members will then use the codebook to independently code the compiled user profiles while a third team member will review these sections of coded data and resolve discrepancies. A random sample of 20-40 instances will be drawn for the coders to begin with and calculate an inter-rater reliability score based on their code assignments. If this score is <95%, we will refine the codebook definitions and re-train the coders. Coders will then complete the coding of the remaining instances and we will calculate an inter-rater reliability score. Discrepancies will then be reviewed and resolved by the research team.[74] We will use Dedoose software to assist with theme identification, coding textual data, and describing relationships among codes (via code co-occurrence and memoing functions). Coding and analytic activities will be discussed during weekly team meetings. These data will allow us to make final refinements to the app as well as

the intervention protocol and assessment battery prior to initiation of the open technical evaluation (Aim 2) and RCT pilot (Aim 3).

10.3.2 Aim 2: Open Technical Pilot

Each participant will be given access to the app for 2 months. Following this period, they will be asked to complete a survey on intervention satisfaction and an online exit interview. We will solicit feedback about the acceptability and utility, and assess how the app and intervention components could be strengthened, identifying areas needing improvement for future iterations. Participant feedback will be specifically sought on the subjective impact of the app on study outcomes. Participant feedback will also be solicited on the acceptability of the assessments with respect to duration and relevance.

Intervention satisfaction will be assessed using the mean score on the System Usability Scale (SUS), a validated 10-measure scale that assesses subjective usability of a system, or, in this case, an app. It is scored from 0 to 100, and a score of 50 or greater indicates that the app is acceptable.

A rapid analysis of the data from the exit interviews will be conducted by the PI team at Fenway Health using the detailed notes taken on the Exit Interview Summary CRF. Additionally, the iTech Analytic Core will assist with more in-depth coding of the data from the exit interviews. A codebook of a priori and emergent themes, including operational definitions of all codes and sample quotations to illustrate how to apply each code, will be created. Two study team members will then use the codebook to independently code the compiled user profiles while a third team member will review these sections of coded data and resolve discrepancies. A random sample of 20 instances will be drawn for the coders to begin with and calculate an inter-rater reliability score based on their code assignments. If this score is <95%, we will refine the codebook definitions and re-train the coders. Coders will then complete the coding of the remaining instances and we will calculate an inter-rater reliability score. Discrepancies will then be reviewed and resolved by the research team.[74] We will use Dedoose software to assist with theme identification, coding textual data, and describing relationships among codes (via code co-occurrence and memoing functions). Coding and analytic activities will be discussed during weekly team meetings.

After analyzing both the qualitative and quantitative data from the open technical pilot (as described above), we will triangulate the findings in order to refine the app, intervention protocol, and assessment tools prior to the RCT pilot (Aim 3). The study team will meet to discuss themes that emerged in the qualitative interview exit interviews, usage patterns, and acceptability ratings, and obtain staff input in order to come to a consensus on specific adaptations that need to be implemented for Aim 3.[75]

10.3.3 Aim 3: RCT Pilot

The primary analyses will summarize acceptability (mean score on the SUS) and feasibility (participants utilizing the app at least once during follow-up) of the app at 3-month follow up, overall for the intervention arm, with asymptotic normal 95% confidence intervals. Point estimates for mean acceptability ≥50 and for proportion accessing the app >0.60 will be considered the minimum criteria for acceptability and feasibility, consistent with industry standards.[64, 65]

The primary efficacy analysis will compare HIV testing (defined by the proportion that self-report at least one HIV test result during follow-up) between the study arms. Secondary analyses will examine group differences in self-reported PrEP-related appointments and documented (e.g., via MRA) HIV test results. Moreover, group differences in measures related to the SCT model constructs (e.g., HIV testing self-efficacy) will be assessed. All analyses will use two-tailed tests of significance, with significance at alpha = 0.05. We will follow an intent-to-treat model, analyzing participants in the study arm to which they were assigned. We will examine the equivalence of random assignment to groups with regards to key baseline characteristics, including socio-demographics, prior HIV testing patterns, and sexual risk-related variables. In the event that randomization does not work to balance these characteristics, we will assess whether baseline differences may account for differences in outcomes.

A rapid analysis of the data from the 3-month qualitative interviews will be conducted by the PI team at Fenway Health using the detailed notes taken on the Interview Summary CRF. Additionally, the iTech Analytic Core will assist with more in-depth coding of the data from the interviews. A codebook of a priori and emergent themes, including operational definitions of all codes and sample quotations to illustrate how to apply each code, will be created. Two study team members will then use the codebook to independently code the compiled user profiles while a third team member will review these sections of coded data and resolve discrepancies. A random sample of 20 instances will be drawn for the coders to begin with and calculate an inter-rater reliability score based on their code assignments. If this score is <95%, we will refine the codebook definitions and re-train the coders. Coders will then complete the coding of the remaining instances and we will calculate an inter-rater reliability score. Discrepancies will then be reviewed and resolved by the research team.[74] We will use Dedoose software to assist with theme identification, coding textual data, and describing relationships among codes (via code co-occurrence and memoing functions). Coding and analytic activities will be discussed during weekly team meetings.

Note: Any deviations from the analysis plans outlined above or in the sections that follow will be documented and justified in the Statistical Analysis Plan developed for this protocol.

10.4 Missing Data

Several procedures will be used to conduct data analysis when data for either outcomes or covariates are missing. The first step will be to assess the extent and pattern of missing data. If data are missing for only a few cases, then data analysis will be conducted only on study participants with complete data. However, when such a strategy would result in loss of data from a substantial proportion of participants, or if this approach would lead to biased or inaccurate results, then some form of imputation will be performed. The form of imputation used will depend on the nature of the data that are missing. For example, data that are collected repeatedly might be imputed using the “last value carried forward” method; and in some instances, interpolation between neighboring points might also be used. When the primary endpoint is missing, one data analysis will be conducted using only cases with the endpoint. Subsequent analysis will be done where missing endpoints are imputed. Hot-deck imputation or regression imputation may also be used in this context.

11.0 HUMAN SUBJECTS

This study will be conducted in compliance with the protocol, ICH Good Clinical Practice guidelines, and 45 CFR Part 46.

11.1 Participants' Confidentiality

All records with personally identifying information will be kept in a locked, limited access area (such as a locked file cabinet) or in a secure limited access database (such as SMART). All computer entry and networking programs will be done with coded numbers only. Clinical information will not be released without written permission of the participant, except as necessary for monitoring by the MC or NICHD.

Every effort will be made to ensure that study participants are protected from risks.

Breach of Confidentiality: A potential risk to participants is violation of confidentiality. We will take the utmost caution to protect the confidentiality of all responses. We will minimize this risk by maintaining confidentiality and discretion throughout all iTech research procedures and data management and analysis.

All audio files will be kept confidential and stored in a limited access folder on Box, accessible only to study staff. All members of the research team will be trained in confidentiality and have signed confidentiality agreements. A professional transcription service, experienced in the handling of confidential data, will be used to fully transcribe verbatim all audio files. Prior to receipt of the first audio file, the transcription service will be instructed to exclude from the typed transcript identifying information (e.g., a name) that may have been verbalized during the course of the theater testing focus groups.

All in-person study visits will be conducted in a private room. Hard and soft-copy participant data with be identified by an ID number only, and a link between names and ID numbers will be kept separately under lock and key. Locator information and informed consent/assent will be filed in designated name files. Provided they contain no identifying information, clinical data may be stored together with other data forms. Otherwise, the data and forms will be filed separately. Soft copy data will be stored on study-specific secure and password-protected network drive folders and will only be accessible to study staff. Hard copy data are stored in locked cabinets within restricted and secure areas at study sites. The study site will maintain all study documentation for at least five years after the completion of the study. Study staff at all sites are trained in confidentiality and have signed confidentiality agreements. Study staff have been trained in ethical human subjects research techniques in order to minimize participant risk as much as possible. From our experiences, these methods have proven to be effective to protect against risks.

Responses to the assessments will be recorded anonymously and transmitted over the internet using industry-standard SSL encryption technology (the same technology used for online banking). The names and contact information of participants will not be collected at this time. Survey responses will remain anonymous and will not be linked to individual participant's names or contact information at any point during the study.

Participants interested in ordering home STI testing kits (i.e. CareKits) or condoms/lubricants will be directed to a separate data collection instrument on SurveyGizmo. After selecting the items they would like to order, participants will be asked to provide names, mailing addresses, and preferred contact information (email or cell phone number for SMS). This personal information will be used only for the purposes of fulfilling the order, confirming participation in the study and returning lab testing results, and will be kept in a password-protected file on a secure drive. STI testing lab results will be posted to HIPAA-compliant web-based platform SMART in Aim 3 for participants to access (see Section 7.4.4 for more information on SMART).

11.2 Certificate of Confidentiality

This research specifically targets a vulnerable population, children (YMSM ages 15-17). We will take every available step to minimize the risk of identifying/linking data being subpoenaed, stolen, or inadvertently released. First, the iTech will request a Certificate of Confidentiality from the NIH. Second, all research staff members are required to complete ethical clearance certification regarding protection of human's subjects through their relevant IRBs. Third, all studies will have documented procedures to safeguard against the risk of the linking information being stolen by keeping such information in a locked spaces to which only essential study personnel who have completed CITI certification for human subjects research ethics training (http://citiprogram.org) will have access.

A Certificate of Confidentiality for the iTech will be sought prior to enrolling participants. As noted on the NIH website (http://grants.nih.gov/grants/policy/COC/faqs.htm#187), a Certificate of Confidentiality will help the research team "...avoid compelled 'involuntary disclosure' (e.g., subpoenas) of names and other identifying information about any individual who participates as a research subject (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect." We have applied for and received Certificates of Confidentiality for other NIH-funded research projects, and given the sensitive nature of the data collected for this project, do not foresee difficulty securing one for this study.

11.3 Risks and Benefits

11.3.1 Risks

Risks to participants in this research study may include:

The measurements that are involved in this study require fingerstick to collect blood samples. This procedure may cause local discomfort, bleeding, or bruising; rarely small clot or infection can occur at the blood draw site. This measurement should not be considered greater than minimal risk in and of itself given its routine use in general health care delivery.

To minimize the risk of participants feeling uncomfortable about answering personal questions, we will use Computer-Assisted Self Interview (CASI) methods for the study's surveys. In CASI, participants read survey questions on a laptop computer or mobile phone and use a

combination of mouse click and keyboard/touchscreen entry to input the answers themselves. Study staff may be available to assist participants with questions or technical difficulties on the CASI. Participants will also be able to refuse to answer any question that makes them uncomfortable.

To minimize risks to confidentiality, we will secure study data with all appropriate physical, electronic, and operational protections. Data will be stored in a physically secure environment. All data files will have encryption and strong password protection. Any identifiable data will either be stored on Emory University's secure servers, on fully encrypted computers, or on paper forms securely stored at the study sites. CASI surveys and online eligibility screening will take place on an encrypted commercial survey website, SurveyGizmo (http://www.surveygizmo.com/survey-software- features/secure-link/). This site has been used by the investigators for thousands of online surveys with MSM with no data security breaches. Access to data will be on a role-based standard; only those study staff who require access to each type of data to complete their study-related roles will be allowed access. All study staff will be trained in security and confidentiality procedures, and will sign a confidentiality agreement before receiving access to any participant data.

We will also develop procedures to minimize indirect disclosure that a participant is participating in an HIV- related research study, or a study that enrolls MSM. For each mode of contact information, we will ask specifically whether anyone else potentially has access to that mode of communication, and if it is acceptable to leave a non-specific message about participation in a health study. No study-related messages will ever mention HIV prevention or the nature of the research study. Additionally, all scripts for email, text message, and telephone contact with participants will be reviewed and approved by the UNC-CH IRB before being used for contact with participants.

We use SSL encryption for transfers of information online, and SurveyGizmo has a business partner HIPPA agreement with Emory. SurveyGizmo’s servers are HIPAA compliant.

The Analytic Core will use Dedoose software to perform all qualitative analyses. Dedoose is a web-based application for organizing and analyzing textual, audio, and video data (qualitative) along with outstanding functionality for their integration with survey, test score, ratings, and demographic data (quantitative). Dedoose employs the highest levels of data encryption available for a web application in all data storage, back up, and transmission. Dedoose allows for a project specific encryption feature. When using this feature, only Dr. Muessig or her designee will hold the additional encryption key needed to be entered in order to view the project. This gives Dr. Muessig exclusive control over who can view the project under any circumstances.

In addition to a Certificate of Confidentiality, we will protect participants in the following ways:

1. Breach of confidentiality. We will take every precaution to minimize risks to study participants. All AC research staff members are required to complete ethical clearance certification regarding protection of human subjects through UNC-CH or Emory University. We also have a strong data and safety monitoring plan in place to protect participants. Adverse events will be reported to the UNC-CH and Emory IRBs, individual research PI institutional IRBs and SRV site-specific IRBs per each institution’s IRB reporting requirements using Adverse Event Reporting Forms

created by the Analytic Core (AC). When possible, reports will be sent within 24 hours of notification by the PIs. Annual updates on enrollment and retention will also be sent to the IRBs.

All data collection will take place in secure and supervised clinical settings. All study personnel names on this application have completed training and received certification in Human Subjects Research Protection (CITI Program) and HIPAA regulations. They will continue to renew this training in compliance with institutional policies.

11.3.2 Benefits

Few direct benefits to participants are anticipated in the theater testing focus group discussions. However, the participants may feel good about themselves as a result of helping researchers address issues related to HIV prevention for YMSM. If the app is successful at increasing HIV testing and PrEP uptake, those receiving the intervention may benefit from increased receipt of HIV prevention services.

11.4 Institutional Review Board (IRB) Review and Informed Consent

This protocol, the informed assent/consent documents and any subsequent modifications will be reviewed and approved by the UNC-CH IRB who is responsible for the oversight of the study. The informed assent/consent will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation.

Written informed assent/consent will be obtained from the participant for Aims 2 and 3. The signed original assent/consent form for Aims 2 and 3 will be kept on file at the SRV site, and a copy of the assent/consent form will be given to the participant. Sample informed assent/consent forms are included with IRB submission.

11.5 Waiver of the Requirement for Parental Permission for Special Circumstances

For all aims of the study, the UNC-CH IRB will be requested to grant a waiver of parental permission to participate in this research study for youth participants under the age of 18.

Under 45 CFR 46.408 (c), an IRB has the authority to waive parental permission if it determines that “a research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects” and “an appropriate mechanism for protecting the children who will participate as research subjects is substituted” and “that the waiver is not inconsistent with Federal, State, or local law.”

A waiver of parental permission for studies with lesbian, gay, bisexual, transgender and questioning (LGBT) youth that do not involve greater than minimal risk is a common practice among researchers working in the area of gay and lesbian health/mental health. This is done to avoid the selection biases operating in only recruiting youth whose parents are both aware of and comfortable with their sexual orientation. Commonly these youth have explored their sexual orientation without their parents’ knowledge as the youth struggle with issues of disclosure and its consequences within the social, religious, and economic context of their families. A

requirement for parental permission in this type of study could not only affect a person's willingness to participate, but could also potentially impact the ability of researchers to engage in this type of research with sexual minority youth.

If the purpose of requiring parental permission as stated in CFR is to protect the minor subject, then requiring parental permission for youth in these circumstances is not a reasonable requirement. Additional privacy protections are provided in that all assessments, notes, reports, and other records will be identified by only a coded number to maintain participant confidentiality. These records and any forms that do contain identifying information (e.g., assent/consent forms, contact information) will be kept in a locked, limited access area (such as a locked file cabinet) at the participating study sites.

11.6 Waiver of the Requirement for Signed Consent Form

11.6.1 For Study Participation

For Aim 1 theater testing focus groups, we will be applying for a Waiver of Written Documentation of Informed Consent to obtain just a verbal consent from participants prior to participation in the focus group. This aim of the study is minimal risk and identifying information will only be collected for scheduling appointments (and not connected to any data) since no follow-up is required. A written assent/consent form will be reviewed with each potential study participant and provided to each assenting/consenting one. This form describes the purpose of the study, the procedures to be followed, and the risks and benefits of participation.

Pending IRB approval, the specific requirement for written informed consent (i.e., each participant's signature) will be waived per U.S. Code of Federal Regulations Title 45 Part 46 Subpart A Sections 46.116(d):

"(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that":

1. The research involves no more than minimal risk to the subjects.

It is unlikely that participants will be at any risk for harm as a result of study participation. No identifiers or contact information will be collected as a part of the focus groups; thus, obtaining a signature as a part of the informed consent process would increase risk for participants. Further, no other identifiers are necessary since participants will not be followed after the focus groups and there is no need for locator forms or any other collection of identifying information.

2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.

The waiver of each participant's signature will not affect the standard and reasonable protections afforded all research participants. Participation in the focus groups is

completely voluntary. Participants may decide not to take part or to withdraw from participation at any time without penalty or loss of any benefit to which they are otherwise entitled. The specific names of participants will not be recorded or made public at any time during the study, including publication of findings. None of the information will become part of any medical record, and all study records will be strictly maintained according to current legal requirements.

3. The research could not practicably be carried out without the waiver or alteration.

Because we do not collect identifying information as a part of the focus groups, a written consent would require additional identifying information that could potentially link subjects to their participation in the study.

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

For study-related questions or concerns, information to contact study staff and the IRB will be made available to the focus group participants. Additionally, all results from this study will be published in academic journals which are accessible to members of the public, including those who participated in the study.

11.7 Prisoner Participation

NICHD has concluded that this protocol does NOT meet Federal requirements governing prisoner participation in human subject research and should NOT be considered by the UNC-CH IRB for the recruitment of prisoners. Subjects enrolled who subsequently become incarcerated or are placed in detention may not continue study participation. Study visits cannot be conducted during the period of incarceration or detention.

11.8 45 CFR Parts 160 and 164 Standards for Privacy of Individually Identifiable Health Information ("Privacy Rule" Pursuant to the Health Insurance Portability and Accountability Act - HIPAA)

Each study site is responsible for adherence to their individual institution's HIPAA policies and procedures.

11.9 Repository Policies (if applicable)

11.10 Study Discontinuation

This study may be discontinued at any time by the UNC-CH IRB, NICHD, or other government agencies as part of their duties to ensure that research participants are protected.

12.0 PUBLICATION OF RESEARCH FINDINGS

Any presentation, abstract, or manuscript will be made available for review by the study sponsor(s) prior to submission.

13.0 BIOHAZARD CONTAINMENT

As the transmission of HIV and other blood borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate blood and secretion precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by the Centers for Disease Control and Prevention. These procedures can be found at www.cdc.gov.

Specimens will be transported in accordance with Federal and local laws, and in compliance with OSHA blood-borne pathogens standards. *This policy includes the samples being transported by ground to the local laboratory.* Compliance will be achieved by education of personnel involved with packaging and transporting specimens.

All infectious specimens must be shipped as Diagnostic Specimens according to current IATA Shipping Guidelines for Infectious Substances Class/Div. 6.2. Refer to individual carrier guidelines (e.g. FedEx, Airborne Express) for specific instructions.

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