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ATN 140 - LYNX: A Novel Mobile App to Support Linkage to HIV/STI Testing and PrEP for Young Men who have Sex with Men

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Protocol Chair: **Albert Liu, MD, MPH**

Protocol Vice-Chair: **Hyman Scott, MD, MPH**

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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.

Investigator of Record: _____
Print/Type

Signed: _____ Date: _____

Title: _____

PROTOCOL TEAM ROSTER

Co-Investigators
Albert Liu, M.D., MPH
Clinical Research Director
Bridge HIV, San Francisco Department of Public Health
25 Van Ness Avenue, Suite 100
San Francisco, CA 94102
Albert.liu@sfdph.org
(p) 415-437-7408

Hyman Scott, M.D., MPH
Medical Director, Clinical Research
Bridge HIV, San Francisco Department of Public Health
25 Van Ness Avenue, Suite 100
San Francisco, CA 94102
Hyman.scott@sfdph.org
(p) 415-437-7483

Susan Buchbinder, M.D.
Director
Bridge HIV, San Francisco Department of Public Health
25 Van Ness Avenue, Suite 100
San Francisco, CA 94102
Susan.buchbinder@sfdph.org
(p) 415-437-7479

Site Principal Investigators

Patricia Emmanuel, M.D.
Site PI
2 Tampa General Circle
5th Floor, Ste 5016
Tampa FL 33606
pemmanuel@health.usf.edu

Temitope Oyedele, M.D.
John H. Stoger, Jr. Hospital
toyedele@cookcountyhhs.org
(p) 312-864-4590

Study Coordinators
Kenneth Coleman, M.A.
Study Coordinator
Bridge HIV, San Francisco Department of Public Health
25 Van Ness Avenue, Suite 100
San Francisco, CA 94102
Kenneth.coleman@sfdph.org
(p) 415-437-7443

Kelly Bojan, DNP, APN, C-FNP
Study Coordinator
2020 W. Harrison Street
Chicago, IL 60612
kbojan@sbcglobal.net
(312)-572-4571

Amayvis Garcia, Medical Assistant
Research Coordinator
University of South Florida Department of Pediatrics
17 David Blvd., Suite 200
Tampa, Fl 33606
arebolle@health.ucsf.edu
(p) 813-259-8652

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AC	Analytic Core
AIDS	Acquired Immunodeficiency Syndrome
AE	Adverse Event
AES	Advanced Encryption Standard
ATN	Adolescent Medicine Trials Network for HIV/AIDS Interventions
AWS	Amazon Web Services
BAA	Business Associate Agreement
CASI	Computer Assisted Self-Interview
CFR	Code of Federal Regulations
CRF	Case Report Form
CSQ	Client Satisfaction Questionnaire
DHHS	U.S. Department of Health and Human Services
EC	Ethics Committee
FG	Focus Group
GCP	Good Clinical Practices
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HTTPS	Hyper Text Transfer Protocol Secure
IATA	International Air Transport Association
ICH	International Conference on Harmonization
IDI	In-Depth Interview
IMB	Information, Motivation, Behavior
IP	Internet Protocol
IRB	Institutional Review Board
LGBT	Lesbian, Gay, Bisexual, Trangender
MC	Management Core
MCU	Multipoint Control Unit
MSM	Men who have Sex with Men
NICHD	National Institute of Child Health and Development
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
PI	Principal Investigator
OHRP	Office of Human Research Protection
OSHA	Occupational Safety and Health Administration
PrEP	Pre-Exposure Prophylaxis
QA	Quality Assurance
QNS	Query and Notification System
RDC	Remote Data Capture
RCT	Randomized Controlled Trial
RSA	Rivest, Shamir, and Adelman
Sex Pro	Sexual Health Promotion
SID	Study Identification Number
SMART	Study Management and Retention Tool
SQL	Structured Query Language
SRV	Subject Recruitment Venue

SSL	Secure Sockets Layer
STI	Sexually Transmitted Infection
TC	Technology Core
UNC-CH	University of North Carolina, Chapel Hill
VPN	Virtual Private Network
YMSM	Young Men who have Sex with Men

STUDY ABSTRACT

DESIGN:	*The LYNX protocol will involve qualitative formative work, through focus groups and in-depth interviews (aim 1) and an open technical pilot (aim 2) to refine the LYNX app; and a pilot randomized controlled trial (RCT) to evaluate preliminary acceptability, feasibility, and preliminary efficacy (aim 3) of the LYNX app.*
DURATION:	*Formative work (aim 1) will be conducted over 3-6 months. The technical pilot (aim 2) will be enrolled over a 2 month period, and study follow-up will be 2 months. The pilot RCT (aim 3) will be enrolled over 3 months, and study follow-up will be 6 months.*
SAMPLE SIZE:	*Aim 1 will include approximately 40 HIV-uninfected young men who have sex with men (YMSM). Aim 2 will include up to 15 YMSM. Aim 3 will enroll 60 YMSM, with 40 YMSM randomized to receive LYNX, and 20 YMSM randomized to receive standard of care. Total sample size for this project will be up to 115 YMSM.*
POPULATION:	*HIV-uninfected YMSM between the ages of 15-24, assigned male sex at birth and male-identified, enrolled at two study sites in Chicago, IL and Tampa, FL.*
STRATIFICATION:	*Participants in the pilot RCT will be randomized 2:1 to receive the LYNX app (N=40) vs. standard of care (N=20)*
DATA COLLECTION:	*Data in the formative phase (aim 1) will include videotaped focus groups and in-depth interviews with YMSM. Data from the technical pilot (aim 2) will include an online qualitative exit interview, a computer-assisted self-interview (CASI), and app analytics. Data from the pilot RCT (aim 3) will include CASI, app analytics, case-report form (CRF) data on study implementation, and in-depth interviews in up to 20 participants in the LYNX arm.*
OBJECTIVES	*1) To conduct qualitative, formative work to refine a mobile phone app, LYNX, to promote HIV/STI testing and PrEP uptake among YMSM* *2) To conduct a technical pilot to optimize LYNX app functionality, technical performance, and user satisfaction* *3) To conduct a pilot RCT to evaluate the feasibility and acceptability of LYNX to increase HIV/STI testing and PrEP uptake among YMSM*

Study Design or Schema

Figure 1: Study overview

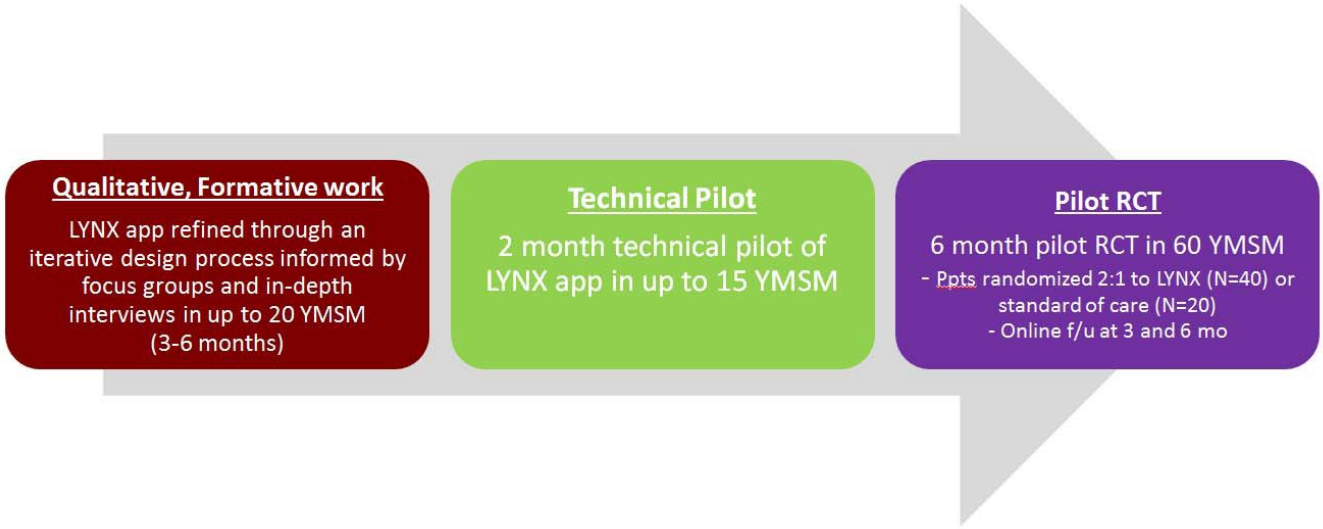
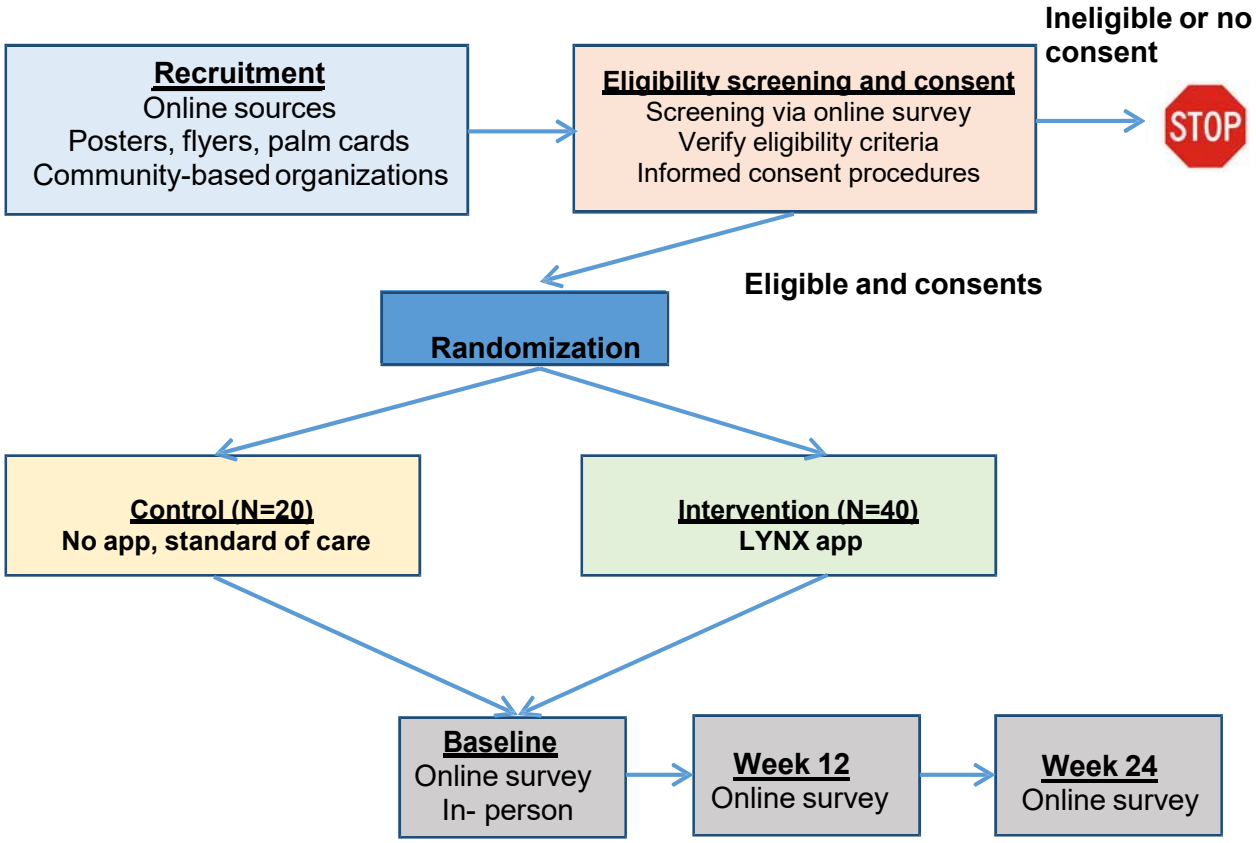


Figure 2: Phase 3, RCT Pilot Study Schema



1.0 INTRODUCTION

1.1 Background

The HIV epidemic has been worsening among young MSM (YMSM). YMSM aged 13-24 had the greatest increase (26%) in diagnosed HIV infections from 2008-2011[1], and infection rates have remained high through 2014. YMSM accounted for 28% of new HIV infections among MSM and 82% of new HIV diagnoses among youth aged 13-24 in 2014.[2] YMSM of color are disproportionately affected by HIV, with Black YMSM experiencing the largest increase in new infections during this period. In 2014, Black and Latino MSM accounted for 55% and 23% of infections among YMSM respectively.[2] There is urgent need for ensuring access to effective HIV prevention approaches in this vulnerable population.

HIV testing is critical for ensuring access to timely treatment and preventing ongoing transmission for HIV-infected YMSM, and for linkage to effective preventive tools for those who test HIV-negative. Although the CDC recommends at least yearly HIV testing for MSM, in a recent national online survey, only 53% of YMSM reported testing in the past year, and 33% had never tested in their lifetime.[3] Only 41% of US HIV-infected youth are aware of their diagnosis, of which only 62% engaged in care within a year.[4] Reasons for not testing include low perceived risk (42%), fear of testing positive (20%), and not having time to test (11%).[5] Bacterial STIs have been identified as potential drivers of HIV infection.[6-16] Despite YMSM having the highest annual STI rate among any age group,[17] STI screening rates are low, with less than half of YMSM reporting STI testing in the last year.[5,18-25] Low perceived risk, lack of symptoms, and lower access to healthcare providers have been identified as barriers to HIV/STI testing.[26,27]

Pre-Exposure Prophylaxis (PrEP) has demonstrated high efficacy, but uptake has been low among YMSM. The iPrEx trial, in which half the participants were under 25, demonstrated an estimated >90% PrEP efficacy among MSM with detectable drug levels in blood.[28,29] Despite these results, there have been myriad challenges to increasing PrEP uptake in the US, including low awareness, concerns about side effects, low risk perception, and PrEP stigma.[30-33] According to national prescription data, youth under 24 are the least likely to initiate PrEP, with only 9% of PrEP initiations in 2015 occurring in this age group.[34] In a recent national survey, only half of YMSM aged 15-24 had heard of PrEP, and 1.7% had ever used PrEP.[35] Demonstration projects also highlight challenges with PrEP uptake. In the US Demo Project of 550 MSM, only 20% were age 25 or under, and PrEP uptake was lower among younger, non-white, and less educated persons. Self-perceived risk was low among those declining PrEP, despite high rates of condomless sex and STIs in this group.[36] In the ATN 110 study of YMSM aged 18-22, PrEP uptake was only 16%, and PrEP adherence was lower among Black YMSM and declined overall during follow-up, particularly with less frequent visits.[37] Taken together, these data point to deficits in self-perceived risk which may result in low PrEP uptake, especially among YMSM of color, and the importance of engaging youth when offering and delivering PrEP.

Mobile technologies have enormous potential to reach and engage YMSM in HIV prevention.[38-42] Mobile phones have nearly reached saturation among youth, making mobile technology a particularly promising tool to reach this population that has been traditionally hard to reach through clinical services. Smart phone adoption is particularly high among young adults, with approximately 86% of those under age 30 owning a smart phone. Youth are more likely to use their mobile devices for more activities, such as downloading mobile apps, Internet access, social networking, and accessing health

information.[43,44] The expansion of smart phones has increased the possibilities of dynamic, mobile phone-based HIV prevention interventions.

Using the Information-Motivation-Behavior Skills (IMB) model, we have developed a highly interactive mobile app to promote accurate risk perception and increase HIV/STI testing and linkage to care among YMSM. Sex Pro (Sexual Health Promotion) is an innovative web-based tool that provides a personalized HIV risk score, based on data from several large MSM cohort studies.[12,16,45,46] This score is displayed on a "speedometer" (1-20 scale), with a higher score representing a higher level of protection, and was highly predictive of HIV risk among Black MSM in HPTN 061, with all HIV infections occurring in individuals with a score below 16.[47] YMSM found it particularly useful and informative, but preferred a mobile app. Sex Pro has been developed into a mobile app, with additional features incorporated, including a sex diary to facilitate accurate data collection; HIV/STI testing information and reminders; and access to home HIV/STI testing options and geospatial-based testing site and linkage to HIV care information.

This study is part of the iTech NIH U19, which has the overall goal to develop innovative technology-focused interventions addressing the HIV prevention and care continuum for youth.

In this pilot project, we propose to develop a new app, LYNX, by leveraging our existing mobile app platform Sex Pro and incorporating key components for increasing PrEP uptake and refining this app to maximize acceptability among YMSM. We will then evaluate the acceptability and feasibility of this integrated app in a pilot randomized controlled trial (RCT) among YMSM at risk for HIV acquisition in the US. If found to be feasible and acceptable, LYNX will be tested for efficacy in increasing HIV testing and PrEP linkage in a separate efficacy RCT study as part of the iTech.

1.2 Rationale

A mobile app that promotes HIV/STI testing *and increases PrEP uptake* will likely have the largest impact in YMSM. While HIV/STI testing are important first steps in the prevention cascade in YMSM, access to highly effective interventions (e.g., PrEP) are critical for this vulnerable population. Therefore, in this pilot study, we propose to expand our current mobile app to include components to increase uptake and linkage to PrEP for YMSM. Key components of this new integrated app, LYNX will address information, motivation, and behavioral skills (IMB) needs for both increasing HIV/STI testing frequency and PrEP uptake (Figure 1).

Figure 1: LYNX components to increase HIV/STI testing and PrEP uptake, according to the IMB model

Goal	Information	Motivation	Behavioral Skills
Increase HIV/STI testing	● Personalized HIV risk assessment ● Sexual history diary and partner tracking	● Testing reminders linked to HIV risk score. ● HIV/STI testing diary and personalized HIV risk score	● Home-based HIV/STI testing options and instructions ● GPS-based testing site and linkage to HIV care information
Increase PrEP uptake	● PrEP educational materials and links on safety and effectiveness of PrEP	● Testimonials of peers who decided to take PrEP ● Impact of PrEP on Sex Pro score	● Links to youth clinics offering PrEP ● Online tips for insurance/access issues ● Local online PrEP navigators ● PrEP starter

To maximize the input from YMSM in the design of LYNX, this study will begin with formative work through a series of focus groups with YMSM at the sites, which will inform iterative development of the LYNX app. We will then conduct an open technical pilot to identify technical issues, optimize functionality and usability, and increase user satisfaction of the app. We will further refine the app based on these findings and then evaluate the feasibility and acceptability of this app in a pilot RCT. Upon completion of this step-wise study, we will have developed and pilot-tested a highly feasible and acceptable app to increase HIV/STI testing and PrEP uptake among YMSM, which will be ready for testing in a randomized efficacy trial of LYNX and another youth-optimized app (MyChoices) being developed in parallel within the iTech U19, both compared against standard of care.

2.0 STUDY OBJECTIVES

2.1 Primary Objectives:

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

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

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

2.2 Secondary Objectives (Aim 3):

- To compare the rate of HIV/STI testing in the LYNX intervention vs. control arms
- To compare the rate of PrEP uptake in the LYNX intervention vs. control arms
- To compare changes in sexual risk behaviors among YMSM in the LYNX intervention vs. control arms

2.3 Study Hypotheses/Research Questions

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

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

Aim 3: Is the LYNX 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 LYNX vs. the standard of care?

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

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

3.0 STUDY DESIGN

Using an iterative process of app development, this study will be conducted in 3 phases: 1) formative research to refine LYNX with input from YMSM; 2) a technical open pilot to optimize functionality and technical performance; and 3) a pilot RCT to evaluate feasibility, acceptability, and preliminary efficacy of LYNX.

- Formative Phase

Guided by the IMB model, the LYNX app will be refined through an iterative design process informed by a series of focus groups and in-depth interviews in up to 40 YMSM to elicit feedback on content, usability, layout, and functionality of the LYNX app.

- Technical Pilot

The LYNX app will be tested in a 2 month technical pilot study in up to 15 YMSM to optimize app functionality and performance. Data will be used to further refine the app and finalize the intervention protocol, outcome measures, and assessment tools for the pilot RCT.

- Pilot RCT

60 HIV-uninfected YMSM will be enrolled into a 6 month pilot study evaluating the feasibility and acceptability of the LYNX app. Participants will be randomized 2:1 to receive the LYNX app or a standard of care control condition. Feasibility and acceptability will be assessed through app analytics of usage patterns (logins, use of app components) and acceptability scales administered via computer-assisted self interview. We will also evaluate preliminary efficacy by comparing the proportion of YMSM who test at least once during the 6 month pilot, and proportion who successfully link to a PrEP provider, in the intervention versus control groups.

3.1 Study Population

This study will be conducted among HIV-uninfected YMSM aged 15-24 at risk for HIV acquisition for all phases of the study. To ensure inclusion of youth most impacted by HIV, we will oversample YMSM of color, with a goal of enrolling two-thirds of the cohort YMSM of color, and at least one-quarter Black YMSM. 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. While transgender women remain a vulnerable and at-risk population in need of increased HIV testing and PrEP uptake, transwomen will be excluded from this study as the LYNX app was designed for a YMSM population and as such do not meet the needs of transwomen. Additional formative research and piloting required to tailor the tools to transwomen are beyond the scope of this pilot study. The relative small sample size of this trial and small proportion of transwomen who would be expected to enroll would not be able to power any significant statistical findings, and as such, would preclude any scientific contributions to the field specific to this population. Furthermore, passive inclusion of transwomen would effectively do a disservice to this community by merging them into the MSM population when in reality, the two populations have very different needs and characteristics.

3.2 Sample Size

The total sample size for this study is 115 YMSM, with 40 enrolling in the formative phase, 15 in the technical pilot, and 60 in the pilot RCT.

3.3 Study Randomization, Stratification, or Description of Non-Random Assignment Procedures

All participants in the technical pilot will be provided access to the LYNX app. In the pilot RCT, participants will be randomized 2:1 to receive the LYNX app vs. the standard of care. Randomization procedures are further explained in Section 5.2.

4.0 SELECTION AND ENROLLMENT OF STUDY PARTICIPANTS

4.1 Inclusion Criteria

- 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 an iOS or Android mobile phone
- Willing and able to attend an in-person baseline study visit in the Tampa or Chicago area.

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 phase of LYNX 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 LYNX 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 technical 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

Participants will be recruited through a variety of strategies, including online and social media strategies (e.g., Craigslist and Facebook ads); distributing posters, flyers, and palm cards about the study; and direct outreach at local venues frequented by YMSM, including community-based organizations, schools, bars, social clubs, beauty parlors, barber shops, sports venues, churches, health fairs, balls, and other community events. Clinic-based recruitment may include reviewing medical charts of existing patients for potential eligibility, or referrals from other providers in the clinic. In addition, former participants who have previously given consent to be contacted for future research may also be directly contacted for recruitment and screening (described in Section 4.5). 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).

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 potential participants who are at least 15 years of age, the survey will ask for the first name, e-mail, and phone number of the participant. Potential participants who do not meet eligibility criteria will be asked if they would like to be contacted about other research studies. Upon completion of enrollment, potential participants who are ineligible or do not enroll in the study and decline further contact will have their contact information destroyed.

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 procedures

Individuals who screen 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, designated site study staff will complete a Contact Information Worksheet with the participant and/or enter the participant's contact information directly into SMART Web during the enrollment visit. Participants will also be asked to provide social media contact information, if the participant is willing. Participants will be asked to provide a working phone number or valid email address through which they can be reached. Participants will also be asked to provide valid contact information for a family member and/or friend 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 entered into the SMART system and 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

Randomization will be used only for the pilot RCT. Only participants who express interest in using LYNX, meet eligibility criteria, provide informed consent, and complete a baseline assessment will be eligible for randomization. Subjects will be randomized 2:1 into either the LYNX intervention arm (N=40) or control arm (N=20).

The 2:1 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, and stratifed by site (Tampa, Chicago) and age (15-18, 19-24). After consent and baseline survey completion, the participant will be randomized (assigned to the next available random allocation). **LYNX Intervention Condition:** Individuals who receive LYNX 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 provision of information regarding recommendations for HIV testing and referrals to local HIV testing sites and prevention services.

5.4 Intervention/Investigation Procedures

5.4.1 Formative phase (Aim 1)

To refine the LYNX app, we will use an iterative development design with focus groups (FG) and/or in-depth interviews (IDIs) with 8-10 YMSM at each of two study sites, followed over 3-6 months (up to 3 iterations). Using a discussion guide, we will demonstrate the app and wireframes (screenshots) of new components and elicit perspectives in content, layout, usability, and functionality. The IMB domains described above will guide the development process. New content to promote PrEP uptake may include PrEP educational and testimonial videos, curated information and links to PrEP websites and discussion forums (PrEP information); information about how one's Sex Pro score could improve on PrEP (PrEP motivation); a map with PrEP-friendly youth providers, and an online navigator to assist with trouble-shooting PrEP access issues (PrEP behavioral skills). We will also elicit feedback on the HIV/STI testing kit and instructions. We will also investigate preferences for documentation of clinic or home-based HIV/STI testing (release of medical records, taking pictures of test results through app). Participants will be asked to download and test iterative versions of the app for two weeks prior to the next FG or IDI where we will gather feedback on the usability, design, and potential impact of the app. Study staff will use an onboarding document to walk participants through the download procedures and use of the app. FGs and IDIs may be conducted in person, or via video-conferencing. Participants will be reimbursed for completion of each FG or IDI according to local site guidelines.

All FGs and IDIs will be conducted by the LYNX team/study site members and video-recorded for transcription and analysis using Transana software by UCSF/SFDPH study staff. The goal of the analysis is to identify barriers and facilitators to app usability. If available, members of the app development team from Apt Mobility will observe the focus groups via video-conference in case they need more clarification of specific suggestions for improving the app. Analysis of the FG will commence immediately after participants leave in the form of a discussion of salient themes and suggestions among UCSF/SFDPH study staff and the Apt Mobility team. The team will then prioritize changes to the app for the next iteration to be tested and discussed in the next round of focus group discussions. Recordings will be stored on a secure hard drive in a locked cabinet. Analysis of the focus groups in Transana does not require a transcript since the codes are applied to the timeline of the video rather than line numbers in the transcript. If further transcription is necessary, selected segments of the video and audio interview data from the FGs and IDIs will be transcribed by Paul M Garton, Inc., a transcription company with whom we have worked with for the past ten years.

The LYNX app will be refined by **Apt Mobility** (www.aptmobility.com), the development team who created the original version of the Sex Pro app and has extensive experience creating health-related apps with the UCSF mHealth group. The LYNX app will be developed for both iOS and Android platforms simultaneously, the two mobile phone platforms that make up more than 90% of smart phones in the U.S.

5.4.2 Technical pilot (Aim 2)

After revisions to the LYNX app are completed based on the formative phase, we will conduct a 2 month, single-arm, pilot study among 12-15 YMSM across two iTech sites to optimize the technical performance and functionality of LYNX. YMSM who participated in the formative phase may participate in the technical pilot. At an in-person enrollment visit, YMSM will download the LYNX app and answer an online computer assisted self-interview (CASI) questionnaire on sociodemographics, use of

technology, and risk behaviors. Study staff will walk participants through the download procedures and use of the app. Participants will then be encouraged to use all app components over the next two months, including ordering and using the HIV/STI testing CareKit at least once during the technical pilot. 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 study will also request participants 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. Upon completion of the technical pilot, all participants will complete an online exit interview with qualitative-trained study staff to provide feedback on functionality, technical performance, errors and bugs encountered, overall experiences using the app, feasibility and acceptability of methods to confirm HIV testing results, and feedback for further refinement. Online interviews will be conducted using a HIPAA-compliant, video-chat application that provides strong security components and is easy to use across multiple devices. We will also assess preliminary usability and acceptability of the app using the System Usability Scale, a validated assessment tool assessing various domains of the app with demonstrated high internal consistency across a number of studies. Participants will also complete a computer assisted self-interview (CASI) to assess these measures, along with changes in risk behaviors during the study. Participants will be given the option to return to the SRV to complete the online exit interview and CASI or complete them online. Participants will be reimbursed for the enrollment visit and exit interview/CASI according to local study site guidelines. All exit interviews will be recorded and transcribed for analysis.

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 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.

5.4.3 Pilot RCT (Aim 3)

5.4.3.1 Screening and Enrollment

Potentially eligible participants will attend an enrollment visit where eligibility is confirmed, the details of the study will be explained, and informed consent obtained. Participants who participated in formative and/or technical pilot phases of this study will not be allowed to participate in the pilot RCT. Eligible participants will complete a baseline computer assisted self-interview (CASI) of HIV risk behavior, HIV/STI knowledge, utilization of STI/HIV prevention services, PrEP knowledge and attitudes, psychosocial measures (including depression, substance use, stigma, social support), and HIV risk perception and will be enrolled in the study on the same day if possible. Participants will be randomized to receive LYNX (intervention) vs. the standard of care (control) in a 2:1 ratio (see randomization procedures in section 5.2). This design was chosen to maximize collection of acceptability data among app users. Participants who have completed the baseline assessment, have been randomized, and complete app onboarding (intervention arm) or receive the standard of care information about HIV/STI testing and PrEP (control arm) will be considered enrolled in the study. All enrolled participants will receive counseling on the importance of HIV testing per local testing guidelines.

5.4.3.2 LYNX Intervention Arm

Study staff will assist participants in downloading the mobile app, provide instruction on its use, and

help set up reminders to input sex diary entries. Study staff will use an onboarding document to walk participants through the download procedures and use of the app. These reminders will be personalized by the user for day, time, and message content at the first visit, and can subsequently be updated by participants if desired. Participants will be encouraged to explore and use other components of the app, the Sex Pro score, PrEP videos, sexual history diary, chat feature, and geo-location features. Users receive quarterly HIV/STI testing reminders using the mobile device notification feature. For confidentiality purposes, reminder notifications are nonspecific, but inside the app the participant is linked to their customizable testing reminder. Reminders include two options for testing: (1) the ability to order a home HIV/STI testing kit to be mailed free of charge, or (2) a geo-located map of the closest HIV/STI testing sites. PrEP uptake components will be finalized in the formative phase of this study.

5.4.3.3 Control Arm

Participants randomized to the control condition will be instructed to access HIV/STI testing at existing sites in the community. They will be provided with a list of these testing sites, along with an informational brochure about PrEP. All participants will be provided access to Sex Pro (risk assessment tool that is part of LYNX and will be made available online) after completion of the study.

5.4.3.4 Study Follow-up

All enrolled participants will be followed for 24 weeks. After enrollment, all follow-up visits will occur online, with SMS reminders, email, and phone follow-up conducted as needed to ensure completion of study procedures. Participants will complete an online CASI at 12 and 24 weeks and receive a stipend for completion of procedures at each study visit. Visit windows will be approximately 14 days before/after the target date. Participants will also be able to obtain additional home HIV self-test kits during the study follow-up, if needed. At the 3 month visit, any persons who have a positive HIV test plus up to 20 participants randomized to the LYNX arm will participate in an in-depth interview conducted by UCSF/SFDPH study staff via video-conferencing. The purpose of this interview is to elicit feedback on their experiences using the app, any technical difficulties encountered, and how the app could be further improved. 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.”[51] All interviews will be audio recorded for transcription and analysis. Participants will be reimbursed for completion of each study visit according to local study site guidelines.

We will also conduct medical record abstraction for participants in this study. 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. SRV staff will not review the medical records of participants who do not sign a medical record release form. For participants who do sign medical record release form(s), 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.

5.5 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 research staff includes (but is not limited to) an overview of the study, study procedures and human subjects issues (informed consent process, confidentiality), a demonstration of all technology components, 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, Good Clinical Practice, informed consent, quality management, confidentiality, and reporting of adverse events. As appropriate, site research staff will conduct mock visits of study procedures prior to enrollment of study participants.

5.6 Intervention Monitoring/Quality Control

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 phases 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

Below is a summary of the measures for each aim of the study.

6.1 Formative phase (focus groups and in-depth interviews) (Aim 1)

6.1.1 Pre-entry or screening evaluations/measures (online survey)

- *Basic sociodemographics*
- *Eligibility questionnaire*

6.1.2 Quantitative assessment (online/paper assessment)

- *Demographics*
- *HIV/STI testing history, PrEP use history*
- *Sexual Risk and Drug Use Behaviors*
- *Technology use*

6.1.3 Qualitative assessment (Focus group/in-depth interview guide)

- *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 IMB model*
- *Attitudes regarding documenting their testing practices and results through signed medical releases, or sending photos of test results via a secure, HIPAA-compliant website*

6.2 Technical pilot (Aim 2)

6.2.1 Pre-entry or screening evaluations/measures (Online survey)

- *Basic sociodemographics*
- *Eligibility questionnaire*

6.2.2 Pre-intervention (baseline) evaaluations/measures (CASI)

- *Level of PrEP interest*
- *Sexual and drug use behaviors*
- *IMB model constructs for HIV/STI testing and PrEP knowledge, attitudes, motivations,and behavioral skills*
- *Eco-social factors influencing uptake o prevention strategies*

6.2.3 On-Study evaluations/measures

- *Exit interview (qualitative interview)*
    - *Feedback on functionality, technical performance, errors and bugs*
    - *Overall experiences of using app*
    - *Feasibility and acceptability of methods to confirm HIV testing results*
    - *Feedback for further refinement*
- *Follow-up CASI (online survey)*
    - *Acceptability:*
        - *System Usability Scale: 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.*
        - *Sexual and drug use behaviors*

- *App-Specific Measures (app analytics)*
    - *Frequency and duration of app use*
    - *Content and functionalities most and least utilized*
    - *Number of HIV/STI home testing kits, condoms and lube requested*

6.3 Pilot RCT (Aim 3)

6.3.1 Pre-entry or screening evaluations/measures (online survey)

- *Basic sociodemoraphics*
- *Eligibility questionnaire*

6.3.2 Pre-intervention (baseline) evaluations/measures

- *Full sociodemographics*
- *Level of PrEP interest*
- *Sexual and drug use behaviors*
- *HIV/STI testing history*
- *PrEP knowledge*
- *IMB model constructs for HIV/STI testing and PrEP knowledge, attitudes, motivations, and behavioral skills*
- *Eco-social factors influencing uptake of prevention strategies*

6.3.3 On-Study evaluations/measures

- *Accetptability*
    - *System Usability Scale: 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**
    - *In-depth interview (qualitative)*
- *Feasibility: app analytics (frequency of logins, use of LYNX app components)*
    - *We will use app analytics to determine whether at least 60% of individuals randomized to the intervention condition opened the LYNX app at least one time after their initial introduction to the app by research staff**
- *App-Specific Measures*
    - *Frequency and duration of app use*
    - *Content and functionalities most and least utilized*
    - *Number of HIV/STI home testing kits, condoms and lube requested*
- *Preliminary efficacy*
    - *HIV and STI testing frequency*
        - HIV/STI Testing: participants will be asked to self-report on frequency of HIV/STI testing since last assessment. The primary HIV/STI 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.

  - *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. We will also explore the concordance of self-reported prep use with data on PrEP use collected by medical release.*
- *Sexual and drug use behaviors*
- *Access to and utilization of health care*
- *IMB model constructs for HIV/STI testing and PrEP knowledge, attitudes, motivations, and behavioral skills*
- *Eco-social factors influencing uptake of prevention strategies*
- *Potential moderators of the intervention (measured at baseline and follow-up visits)*
  - *Demographics: Age, student status, education level, income, living situation, employment, insurance status, depressive symptoms, anxiety, trauma, and abuse*

*Primary study endpoints

6.3.4 Premature Discontinuation/Off-Study evaluations/measures

Participants enrolled in the pilot RCT who discontinue study participation after the Baseline visit, but prior to the completion of the final study visit, will complete a Premature Study Discontinuation visit within four weeks after the decision to prematurely discontinue from the study is made and will include all week 24 visit procedures as appropriate.

The principal investigator has the authority to withdraw any participant at any time if it his/her opinion that 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.

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

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

Subjects who are prematurely discontinued from the study may be allowed to re-enroll into the study on a casebycase basis. The Protocol Team will review the number of slots opened for replacements on a monthly basis, or more frequently, as needed.

Participants who seroconvert during the study enrollment will not be discontinued from the study and

will continue to have access to the app and its functions.

6.4 Clinical and Laboratory Evaluations

Home HIV/STI testing will be offered as part of the technical and pilot RCT phases of this project. This will include the Oraquick HIV in-home test kit and an STI self-collection kit for urine, pharyngeal, and rectal swabs for gonorrhea and chlamydia testing and a microtube for blood collection for syphilis testing. All specimens will be sent via a mailer with pre-paid postage to the Kraft Laboratory at Emory University, a CLIA-certified laboratory with extensive experience testing home-collected specimens and high sensitivity and specificity (>95%) for home-collected STI testing. Any participant who tests positive on a test from a home specimen collection will be contacted by phone by the study team and provided supportive counseling and referral to treatment services. Positive STI results, including confirmatory HIV, are reported to the local health department, and participants are notified of this in the assent/consent form.

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, 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 participant codewill 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 will be provided by the developer. Original source documents for individual participants will be maintained at the respective SRV 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. Hard copies of CRFs may be ordered from the MC via an order form on

the iTech website.

7.3.2 Study Surveys

Self-administered surveys for the quantitative assessment during formative work, upon completion of the technical pilot, and at baseline, week 12, and week 24 visits of the pilot RCT will be completed by participants on study computers or personal devices via surveys hosted on SurveyGizmo.com. The visit windows (including survey completion) will be approximately 14 days before and after the target date, however surveys may be completed out of window up until the next visit window opens. 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 HIPAA agreement with SurveyGizmo. The participant's unique SID# will be used in order to link the interview responses to the participant's CRF data.

7.3.3 CASI Data Security

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.

7.3.4 Mobile App Data Security

The mobile app will also record participant location in order to identify nearby testing locations, but will not access other private information on the user's mobile phone. We will maintain electronic information on a secure Amazon Web Service Cloud (AWS), a secured environment that supports HIPAA compliance (as well as Business Associate Agreement) and has been approved for US government projects that include highly sensitive personally identifiable information. Information collected through the app will be encrypted while on the mobile phone and during transit to our secure servers; users will access the mobile app through a secure password-protected log-in.

7.3.5 VSee Platform Description

For many of the qualitative interviews being conducted, the Analytic Core 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.

7.3.6 Zoom Platform Description

In addition to VSee, the Analytic Core may use Zoom to conduct qualitative interviews and focus groups remotely. Participants will have the option to conduct face-to-face video chat, video chat in which they can see the interviewer, but the interviewer cannot see them, or audio chat only. Zoom is compatible on PCs, tablets, and smartphones; as well as maintains the option to conduct an audio conference without the video component. University of California, San Francisco has entered into a BAA with Zoom, where Zoom agrees to be responsible for keeping all patient information secure and report any breaches of protected health information (PHI).

End-to-end encryption. Zoom encrypts all presentation content at the application layer using the Advanced Encryption Standard (AES) 256-bit algorithm. Zoom end-to-end (E2E) chat encryption allows for a secured communication where only the intended recipient can read the secured message. Zoom uses public and private keys to encrypt the chat session with Advance Encryption Standard (AES256), and session keys are generated with device unique hardware ID to avoid data being read from other devices. This ensures that the session cannot be eavesdropped or tampered with.

Cloud Control Infrastructure. A distributed network of low-latency multimedia routers (software) resides on Zoom's communications infrastructure. With these low-latency multimedia routers, all session data originating from the host's device and arriving at the participants' devices is dynamically switched — never stored persistently through the Zoom communications infrastructure. Zoom's communications infrastructure for real-time video, audio, and data communications resides on Zoom dedicated servers, which are housed in SSAE 16 SOC2 compliant datacenters on opposite sides of the US. Zoom sessions are completely temporary and operate analogously to the popular mobile conversation over the public mobile network. In addition to unique security benefits, Zoom's communications infrastructure also enables an extremely scalable and highly available meeting infrastructure unrestricted by the limitations of physical data centers.

The Zoom client communicates with the multimedia router to establish a reliable and secure connection. At the time of instantiation, the Zoom client will determine the best method for communication, attempting to connect automatically using udp and tcp port 8801, 8802 and 8804 or HTTPS (port 443/TLS).

The Zoom sessions will contain identifying information, as in VSee above, but this information will be be stripped form the recorded Zoom 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, the LYNX study will use CRFs to collect data on key study visit data (e.g., enrollment and randomization assignment), study milestones such as completion or discontinuation, HIV/STI testing history and 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/Video Data

We will conduct focus groups (FGs) (in Aim 1) and in-depth interviews (IDIs) (in Aims 1, 2, and 3) to evaluate the overall relevance of the app to YMSM and identify ways to adapt specific features of the app to promote STI testing, PrEP uptake and PrEP adherence among YMSM. FGs and IDIs will be conducted in person or using VSee or other HIPAA compliant, IRB approved method for video-conferencing. Video will enable us to better interpret comments about specific features of the interface and to be able to determine who said what over the course of the iterative FGs. All participants will be provided with a pseudonym on a name card placed on the table in front of them and visible on the recording. Audio and video data will be recorded in person using a digital video recorder or using the

recording feature of the VSee or Zoom app that will record audio and video of the FG participants and the shared images of wireframes of the app interface. Audio and video data will be transferred from the recorder or computer to an external hard drive that will be kept in a locked office by UCSF/SFDPH study staff. If necessary, portions of the videos and/or audio that require transcription will be sent to our transcription service, PaulMGarton.com using a secure, encrypted filebox provided by Sendthisfile.com embedded on the PaulMGarton.com site. Transcripts of the FGs and IDIs will not use the names of the participants, only their pseudonyms for FGs or study ID for the IDIs.

7.4.3 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 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.

7.5 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 the LYNX study will develop and adhere to 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 and training concerning the recording of study data on the CRFs, entry of the data into RDC, and CASI administration.

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., consent forms, case report forms) *and pertinent hospital or clinic records* readily available for inspection by the local IRB, 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

All subjects will be contacted up to 2 weeksprior to their target date for a follow-up visit to complete study visit procedures; additional reminders will be provided on/after the target date as needed to ensure completion of study visit procedures. Multiple contact methods will be used for youth who are difficult to reach (e.g., mail, alternate phone numbers, e-mail, text message, social media contact information). 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 IRB of Record (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"

Focus groups, interviews, and surveys will contain questions regarding stigma and other personal experiences, and some participants may be uncomfortable answering certain questions. 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. 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.

If at any time during the study, a participant divulges that he 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 is suicidal/homicidal, measures will be taken to ensure his 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.

9.0 MONITORING UNTOWARD EFFECTS ASSOCIATED WITH OR RESULTING FROM STUDY

Site research 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.

First, the study will catalogue any untoward effect related to the participant as a result of study participation, including use of the LYNX app and home HIV/STI testing. 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 protocol team of these untoward effects using the iTech QNS accessible through the iTech website (www.itechnetwork.org). Study staff will be briefed during the training on the scope of possible untoward

effects and instructed to report events.

Second, 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 Statistical Analysis Plan

10.1.1 Formative Phase (Aim 1)

FGs and IDIs will be conducted in person or remotely using VSee app or Zoom (or other HIPAA-compliant, IRB approved video- conferencing app). The initial FGs will be facilitated by UCSF/SFDPH study staff in person at the iTech sites in Tampa and Chicago. In person IDIs by UCSF/SFDPH study staff may also be conducted during the site visit, schedules and time permitting. Subsequent FGs and IDIs will be conducted using the VSee app to maximize the flexibility of the data collection in the context of iterative app development. If possible, members of the LYNX design and development team may also participate in the follow-up FGs and IDIs to probe about specific features and app preferences. The FGs and IDIs will be video- recorded to capture YMSM feedback and allow ability to distinguish different speakers. Video also provides important contextual information on participant reactions when viewing and commenting on specific features of the app interface. After each interview, a short debriefing form will be completed by the interviewer noting salient comments on usability of existing features, requested features from the interview, and the overall usefulness of the information obtained for iterative design of the app. These debrief forms will serve as a summary of the interviews and will guide the researchers on what videos or parts of the videos to transcribe and/or review for the app developers. The goal of the analysis will be to evaluate the overall relevance of the app to YMSM and identify ways to adapt specific features of the app to promote STI testing, PrEP uptake, and PrEP adherence among YMSM. The team will meet weekly to discuss emerging findings and whether changes to the interview guide are necessary. Data from these focus groups and IDIs will be used to iteratively refine the app, intervention protocol, and assessment tools prior to the technical pilot in Aim 2.

10.1.2 Technical Pilot (Aim 2)

All exit interviews from the technical pilot will be transcribed in full. Qualitative data will be analyzed by iTech Analytic Core staff using the methods described in aim 1 and will inform efforts to further refine the app, intervention protocol, and assessment tools prior to the launch of the RCT pilot. Quantitative data will be used to characterize participants in the technical pilot and provide further information on the usability of the app.

10.1.3 Pilot RCT (Aim 3)

Response rates to follow-up surveys will be tabulated by recruitment venue and respondent characteristics to help understand potential sources of bias. We will characterize the study population using descriptive statistics and compare the intervention and control groups at baseline using t-, Wilcoxon, and chi-square tests. Point estimates for mean SUS score ≥ 50 and for proportion accessing the app >0.60 will be considered the minimum criteria for acceptability and feasibility, consistent with industry standards.[49,50] A secondary feasibility outcome will be achieved if ≥50% of participants who open the app complete their personalized risk score at least once.

The secondary outcomes of preliminary efficacy of the LYNX app to increase HIV/STI testing (any testing over follow-up) and PrEP uptake (as described above) will be evaluated using unadjusted risk ratios for each outcome. If there is evidence of divergence from balance in measured baseline covariates (i.e., failure of randomization), post-hoc analyses using Poisson regression with robust standard errors will be used to estimate adjusted risk ratios. Outcome variables will represent any HIV testing and any PrEP uptake over the follow-up period. Separate models will be estimated for each outcome.[52]

With 60 participants randomized 2:1 to intervention: control, and 10-20% attrition, we will have 80% power to detect 37-42 percentage point increases in HIV testing and PrEP uptake, depending on rates in controls. The lack of precision and large minimum detectable effects, typical of pilot studies, will entail careful interpretation of study results in the light of overall patterns, plausibility, and findings from other mHealth studies.

Qualitative data from exit interviews will be analyzed by the LYNX team using the methods described in Aim 1 and will inform efforts to finalize app revisions and prepare for efficacy evaluation of the app.

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.

10.2 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.

We will inform participants to only use first names or nicknames during the focus groups and that all information discussed during the focus groups will be used to develop general themes and will not be linked to any specific person. The focus groups will be conducted by study team members with extensive experience in ensuring the safe conduct of group discussions. We also ask participants not to discuss any information from the focus groups once they leave. Participants also have the right at any time to decide not to participate or answer questions.

All audio/video 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/video files.

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.

Participants may be concerned about the security of their data, particularly since it is collected and stored electronically. The Analytic Core has significant experience developing security protocols for internet-based studies, and we will take a variety of steps to ensure participant security, including using a dedicated server behind a firewall, encryption of data, separation of identifiers from responses, and password-protected access to data. Therefore, we believe that this risk will be minimal.

All data collected by the LYNX app will be secured through the following security measures: All data stored on a user's device will be encrypted, as will all data stored in the research database. The encrypted MySQL database will be stored in the Amazon Web Service Cloud (AWS), a secured environment that supports HIPAA compliance (as well as Business Associate Agreements) and has been approved for US government projects that include highly sensitive personally identifiable information. All data transfers between a user's mobile device and the research database will be

encrypted and transmitted via Secure Socket Layer (SSL); and external systems will only have access to specific fields (or objects) necessary to accomplish the research objectives. Data download access will be on an as-needed basis to designated individuals within the research organization which may be limited by IP address, further ensuring data is not downloaded by unauthorized parties. All administrative interfaces are accessed through SSL ensuring that data are safe, secure, and available only to registered users.

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. 3 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 fingerstick site. This measurement should not be considered greater than minimal risk in and of

itself given its routine use in general health care delivery.

Participants may also feel discomfort or pain with collection of pharyngeal or rectal STI specimens. This risk will be minimized through providing written and video instructions to participants.

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. In-depth interviews will be conducted face-to-face or online depending on the research project.

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 HIPAA 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 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 Analytic Core 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 using Adverse Event Reporting Forms created by the Analytic Core. 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

There may be no direct benefits to participating in this study. Participants who receive the LYNX app may receive assistance in accessing HIV/STI testing and PrEP, which has been shown to be effective in reducing HIV acquisition. All participants will receive information on how to access PrEP in their local community.

11.4 Institutional Review Board (IRB) Review and Informed Consent

This protocol, the informed consent documents and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for the oversight of the study, the UNC-CH IRB who is acting as the single IRB (IRB of Record) for this study. The informed consent will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation.

Written informed consent will be obtained from the participant. The participant's consent/assent must also be obtained if he is able to understand the nature, significance, and risks of the study. The signed original consent/assent form will be kept on file at the site and a copy of the consent/assent form will be given to the participant.

11.5 Waiver of the Requirement for Parental Permission for Special Circumstances

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. Rationale and procedures for waiver of parental consent are described in section 4.4.

11.6 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.

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

11.8 Study Discontinuation

This study may be discontinued at any time by the NICHD.

12.0 PUBLICATION OF RESEARCH FINDINGS

Any presentation, abstract or manuscript will be made available for review by the study sponsors 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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