MyPEEPS YTM: To Advance HIV Prevention

Sponsored by:
Division of AIDS (DAIDS) United States (US)
National Institute of Mental Health (NIMH)
US National Institutes of Health (NIH)

Multiple Principal Investigators (MPIs):
Rebecca Schnall
Robert Garofalo

Co-Investigators (Co-Is)
Lisa M. Kuhns
Asa Radix

Final Version 1.5
November 09, 2023

TABLE OF CONTENTS

PROTOCOL TEAM ROSTER

Multiple Principal Investigators

Rebecca Schnall, PhD, MPH, RN-BC
Columbia University School of Nursing
212-342-6886
rb897@columbia.edu
School of Nursing
Columbia University
560 West 168th Street
New York, NY 10032

Robert Garofalo, MD, MPH
Ann & Robert H. Lurie Children's Hospital Chicago
312-227-6110
RGarofalo@luriechildrens.org
Center for Gender, Sexuality and HIV Prevention
4711 N. Broadway
Chicago, Illinois 60640

Co-Investigators

Lisa M. Kuhns, PhD (Core Team Member)
Northwestern University Feinberg School of Medicine
312-227-6119
lkuhns@luriechildrens.org
Ann & Robert H. Lurie Children's Hospital of Chicago
225 E Chicago Avenue, BOX 161
Chicago Illinois 60611

Asa Radix, MD (Core Team Member)
Callen-Lorde Community Health Center
212-271-7200
ARadix@callen-lorde.org
356 West 18th Street
New York, NY 10011

LIST OF ABBREVIATIONS

AE	Adverse Event
AES/AES256	Advanced Encryption Standard 256-bit algorithm
ARBA	AIDS-Risk Behavior Assessment
CASI	Computer Assisted Self Interviewing
CDC	Centers for Disease Control
CFR	Code of Federal Regulations
Co-I	Co-Investigator
CRF	Case Report Forms
CUIMC	Columbia University Irving Medical Center
DAIDS	Division of Aids
DSMB	Data Safety and Monitoring Board
E2E	End-to-End
EC/IRB	Ethics Committee/Institutional Review Board
HAL	Hair Analytical Laboratory
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
ID	Identification card
IP Address	Internet Protocol Address
IRB	Institutional Review Board
ISO	Information Security Office
ITT	Intent-to-treat
MCAR	Missing completely at random
mHealth	Mobile Health
MI	Multiple imputation
MPIs	Multiple Principal Investigators
MSM	Men who have sex with men
MyPEEPS	Male youth Pursuing Empowerment, Education, and Prevention around Sexuality
NIMH	National Institute of Mental Health
NIH	National Institutes of Health
nPEP	Non-Occupation Post-Exposure Prophylaxis
PHI	Protected Health Information
PI	Principal Investigator
PID	Participant Identification Number
PrEP	Pre-Exposure Prophylaxis
PRS	Prevention Research Synthesis
PSSUQ	Post-Study System Usability Questionnaire
RCT	Randomized Control Trial
REDCap	Research Electronic Data Capture
SAE	Serious adverse event

SEM	Social Ecological Model
SEM	Structural Equation Modeling
SID	Study ID number
SOC	Standard of care
STI	Sexually Transmitted Infection
TFV	Tenofovir
US	United States
YMSM	Young men who have sex with men
YTM	Young transmasculine men

MyPEEPS YTM: To Advance HIV Prevention

1.1 INTRODUCTION

1.2 Background Information

Transgender men (TM) are at high-risk for acquiring HIV. Growing research on TM clearly demonstrates increased HIV risk and burden, although not as much risk in comparison to transgender women among whom risk and vulnerability to HIV/STIs has been better described, but considerably higher than the general US population. A recent review was among the first to systematically estimate HIV risk and burden in TM in the US. In this review, there was a high prevalence of HIV (3.2%; lab confirmed) and high rates of HIV-risk behaviors, such as sex work (13.1%) and unprotected sexual intercourse (24.5%), which have been strongly associated with HIV acquisition(1). Although the prevalence of HIV is lower in TM as compared to transgender women, having mainly female sexual partners might partially explain the comparatively lower HIV prevalence among TM. Previously undescribed **HIV risk behaviors and contextual factorspoint to the immediate need for the development and testing of HIV prevention interventions** among YTM. More specifically, the overall estimate for STI diagnoses for TM was 28.7%. Co-morbid infection with bacterial STIs increases the risk of transmission and acquisition of HIV(2, 3), and it has been well established that STIs play an important role in HIV infections among cisgender YMSM(4). Further, prevalence of drug use was high with 38.1% of TM reporting illicit drug use.

Importantly, in our community-based sample of 565 TM in NYC, HIV prevalence among TM who have sex with cisgender men only was 11.8% as compared to 3.5% for TM who have sexwith cisgender men and other partners, and 2.1% for TM who have sex with cisgender women only. These data suggest the potential for alarmingly high rates of HIV in TM who have sex with cisgender men in urban settings, which has not been previously described and speaks directly to the public health significance of the proposed research.

Stigma and discrimination have contributed to disparities in access to healthcare services for TM. Studies show TM experience a high burden of discrimination in multiple settings, including healthcare settings(5, 6). In a large study of TM adults, 33% of the sample delayed needed medical care when sick or injured, and 39% delayed routine preventive care. Stigma and discrimination among TM make it less likely for them to seek sexual healthcare(7). Low knowledge of PrEP(1), low rates of PrEP access(8), and low uptake of PrEP(9) among TM suggests the strong need for the development of health prevention interventions delivered outside of traditional

healthcare settings.

Despite biomedical advances in HIV prevention, there remains a dearth of evidence-based, sexual health HIV prevention interventions for TM. More than four decades into the HIV epidemic, the current Centers for Disease Control and Prevention (CDC) compendium of evidence- based interventions (EBIs) for HIV prevention has no evidence-based interventions for YTM. This underscores the need for behavioral HIV/STI prevention interventions targeted to YTM to avert new infections given their increased risk in comparison to the general population. Therefore, there is a critical need to develop and test the efficacy of HIV prevention interventions for YTM, especially those under 18 years of age. We comprehensively looked at the existing EBIs and considered adaptation of those developed for adolescent females, those with family based-approaches, those designed to target racial/ethnic groups, or those developed for MSM; however, we decided on using the MyPEEPS intervention framework because we have preliminary data suggesting that YTM find the intervention to be very usable. Specific areas that are needed for developing this intervention for YTM have been identified that can be achieved through Aim 1 of this proposed study.

MyPEEPS (Male Youth Pursuing Empowerment, Education, and Prevention around Sexuality) is, to our knowledge, the only theoretically-driven intervention in the published literature which has been tested in YMSM under age 18 years and developed with strong formative work among a diverse group of YMSM. MyPEEPS (R34MH079707; PI: Garofalo) was originally developed as a manualized curriculum consisting of 6 interactive group sessions (2 hours each), delivered twice weekly for 3 weeks. MyPEEPS was developed and tested among diverse YMSM ages 16-20 years, including Black, Latino, and White YMSM. The MyPEEPS intervention targets social-cognitive and cognitive-behavioral factors based on best practices for behavior change, emotion regulation, and HIV intervention (e.g., knowledge, self-efficacy, and behavioral skills) within YMSM-specific social contexts. The MyPEEPS scenarios include, for example, those involving emotionally activating and cognitively complex situations involving for partner-specific factors (e.g., older partners), experiences of social stigmatization (e.g., by race and/or sexual orientation), and sexualized contexts (e.g., online sexual partner interaction, under the influence of alcohol or drugs) and specifically address emotional regulation and minority stress which are salient issues facing adolescents at risk for acquiring HIV. Building on this work, our study team translated the MyPEEPS intervention onto a mobile platform for a slightly younger age group, ages 13-18 years, with content delivered through YMSM avatars (e.g., caricature or graphic identity) whose profiles and problems are based on the formative research of the original pilot trial and who manage their sexual health against a backdrop of personal, family-based, and relational challenges. We are now testing MyPEEPS Mobile in a national randomized trial of 761 cisgender YMSM (U01MD011279; MPIs: Schnall and Garofalo) with interim analysis (n=350) supporting preliminary efficacy (see Preliminary Studies).

Benefits of mHealth in HIV prevention interventions. As part of a comprehensive strategy across the continuum of HIV prevention and care, behavioral interventions remain an important tool in the fight against HIV(10). While many HIV prevention interventions have been delivered face-to-face, the emergence of eHealth as a platform for health behavior change provides new opportunities for developing HIV prevention strategies(11). eHealth is a generic term that applies to an increasingly large number of electronically delivered interventions and can include web-based tools including videos, games, chat rooms, and social networking sites as well as text/SMS and e-mail messaging (12). Schnall et al. conducted a review of eHealth HIV prevention interventions in

MSM and found preliminary evidence that eHealth (e.g., SMS, web-based education modules) improves HIV prevention behaviors in MSM but has not been widely developed for or tested in adolescents(13). Studies have also shown that eHealth HIV prevention interventions developed for adult MSM(14-17) are appealing because of their privacy feature and convenience of use(18). **Therefore, delivery of MyPEEPS using mobile technology has the potential to remove many of the barriers to engagement in YTM and improve scalability**(19). *We will adopt recent recommendations for planning of scale up of efficacious mHealth HIV prevention interventions, including formation of a scale-up working group, which will meet regularly to formulate recommendations for future scale up should the intervention proveefficacious.*
In summary, this application proposes to intervene on a population, YTM, among whom evidence of HIV risk is emerging and increasingly well-documented, at an age (15-25 years) of increasing vulnerability by building on our existing MyPEEPS mobile intervention and developing an intervention specific to the needs of YTM. The proposed mHealth approach is well-suited to both reach this relatively hidden population and, if efficacious, scale widely.

1.3 Specific Aims

1) Using qualitative methodology, expert feedback, and usability assessments, develop MyPEEPS Mobile for YTM.
2) Conduct a pilot randomized controlled trial to examine the feasibility, acceptability, and preliminary efficacy of the revised MyPEEPS Mobile App in a sample of 80 YTM (15-25 years) and refine the study methods for a future efficacy trial.
3) Assess predisposing, enabling, and reinforcing factors for MyPEEPS Mobile among YTM through theoretically-guided in-depth interviews.

1.4 Preliminary Research

a) **Development and Pilot Testing of the MyPEEPS Intervention (R34MH079707; PI: Garofalo)**. MyPEEPS is a social and behavioral theory-driven HIV prevention intervention for diverse YMSM, developed by members of our research team, (Garofalo [MPI], Kuhns [Co-I]), using a multi-stage, mixed-method approach. MyPEEPS was based on the Social-Personal Framework (**Figure 1**) (20) and added important psychosocial and contextual risk factors to YMSM risk-taking. The MyPEEPS pilot study evaluated the initial efficacy, feasibility, and acceptability in an ethnically diverse sample (N=101), including MSM under age 18 years, using a randomized controlled design with an active, time-matched control group. There were no significant differences between arms with regard to demographic characteristics. Sexual risk and social cognitive outcomes were assessed at baseline, 6-, and 12-weeks post-intervention. Over the entire follow-up period, intervention participants were less likely than controls to engage in any sexual behavior while under the influence of substances ($p<.05$), and a decreasing trend in unprotected anal sex while under the influence of substances was also observed in this group ($p = .08$), which is an important risk factor for acquiring HIV(21). Thus, the MyPEEPS intervention, a 6-session behavioral intervention tailored to YMSM ages 16-20 years, was shown to be feasible, acceptable, and demonstrated evidence of preliminary efficacy in reducing sexual risk, specifically sexual risk while under the influence of substances(22).

b) **The MyPEEPS Mobile Trial (U01MD011279; MPIs: Schnall and Garofalo).** Our current trial of 700 YMSM has shown promising preliminary results. First, we have successfully reached our recruitment goals. Second, we conducted an interim analysis for the purposes of report to our Data and Safety Monitoring Board and evaluated the preliminary outcomes in the first half (N=350) of our study sample from baseline to 3-month follow-up. Higher self-efficacy for HIV prevention behaviors (p<.001) and more recent HIV tests in the past 3 months (p=0.02) were reported by the intervention group compared to control. The number of condomless anal sex acts was lower among the intervention group for both insertive anal sex acts (p=0.03) and receptive anal sex acts (p=0.0001). These preliminary findings were reported to our Data and Safety Monitoring Board and are very promising for supporting the use of this intervention for reducing HIV risk behaviors in YTM. Finally, and of great relevance to this proposed study, over 800 YTM screened into our study because of their interest, sexual risk, and behavioral vulnerability but were ineligible based on birth sex criteria. *We will use the list of transgender men who we screened as part of their larger efficacy trial, as part of our recruitment efforts for the proposed R34 study.* Further, we published the findings from our formative work in several peer-reviewed publications and presentations(23-27).

c) **In preparation for this application, we conducted formative focus groups with YTM.** We conducted 6 focus group sessions with 49 YTM from 4 sites (8 Birmingham, AL, 17 Chicago, IL, 12 New York, 11 Seattle, WA). In our sample of 49 YTM, 25 had ever had sex with a cisgender guy and 11 had sex with a transgender female (e.g., sex designated male at birth). Over half (27 of 49) feared disclosing their status as a YTM to a doctor or healthcare provider, demonstrating a key barrier to health seeking. Only 24 (49%) had been tested for HIV in their lifetime. Prior to the focus group session, all participants completed all the MyPEEPS Mobile activities on their mobile phones (e.g., the modules designed for the cisgender YMSM in our current trial). Findings from the focus group sessions demonstrated the perceived usefulness of the intervention for YTM, but also highlighted important limitations. One participant stated, “But yes, it was super realisticand just made it less scary just knowing that you could honestly talk to someone like that where it’s totally protected and private.” Another youth described the usefulness of the App and said, “I wished I had found out about that sooner, because I had a STD scare about a year ago, and I had to learn about it in my doctor’s office with my father there, which was absolutely terrifying.” We conducted a follow-up survey after the participants used the App to assess feasibility and acceptability; 82% (N=40) agreed that “Using MyPEEPS willmake it easier to make safer decisions about their sexual health” and “MyPEEPS gave them information and skills needed to avoid situations that make them uncomfortable and put their sexual health at risk of HIV and other STIs.” However salient, limitations to the current App content highlighted the need for the specific tailoring we propose herein, targeting mechanisms of risk specific to YTM. The specific areas that needed to be addressedwere: 1) content related to family planning, 2) sex while transitioning, 3) body parts, 4) body type, 5) gender inclusivity, 6) addition of TM and gender non-binary avatars, 7) social challenges such as stigma, violence, mis-gendering, and transphobia, 8) sexual/relational power dynamics, and
9) educating their partners on their gender identity.

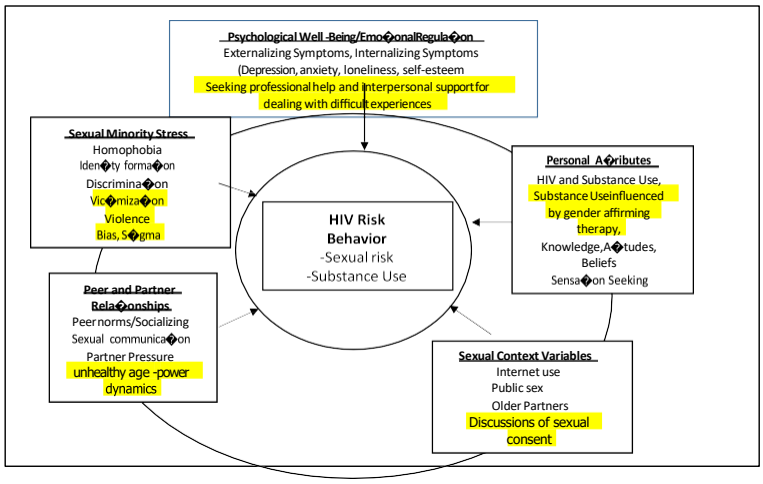
2.1 STUDY DESIGN

We propose to develop a mobile intervention for YTM building on MyPEEPS Mobile, which was originally developed for very young sexual minority men. Central to this intervention is the premise that it will be delivered to youth during a developmental period that precedes or coincides with sexual debut, an important time for intervention, prior to or concurrent with initiation of high-risk behaviors. Given both the gap in HIV prevention science and the lack of current targeted interventions, and building upon our multidisciplinary team's extensive experience in HIV prevention, mHealth, behavioral interventions, randomized controlled trials, and transgender health, we propose the following specific aims: 1) Using qualitative methodology, expert feedback, and usability assessments, develop MyPEEPS Mobile for YTM, 2) Conduct a pilot randomized controlled trial to examine the feasibility, acceptability, and preliminary efficacy of the revised MyPEEPS Mobile App in a sample of 80 YTM (15-25 years) and refine the study methods for a future efficacy trial, and 3) Assess predisposing, enabling, and reinforcing factors for MyPEEPS Mobile among YTM through theoretically-guided in-depth interviews. The proposed MyPEEPS intervention for YTM is a novel and evidence-driven intervention using mobile technology to deliver HIV prevention information to high-risk youth. This will be the first study to develop and pilot a scaled-up, mobile HIV prevention intervention designed by, and piloted for, a diverse group of YTM. The final product of this study will be the basis for an R01 application to conduct a large- scale efficacy study for this population. The proposed MyPEEPS Mobile intervention for YTM is a novel and evidence-driven intervention using mobile technology to deliver HIV prevention information specifically developed for YTM. Consequently, we are confident that the proposed intervention will be of high impact intervention for improving HIV prevention behaviors in YTM and have long-term implications for overall improvement in the public's health.

2.2 Theoretical Framework

Theoretical Framework. The Social-Personal Framework (**Figure 1**) was the theoretical framework that guided the two prior NIH-funded MyPEEPS studies. *The framework has been used broadly for HIV prevention in YMSM, and young women at high-risk for HIV and we now propose to use an enhanced model for guiding our development of MyPEEPS Mobile for YTM. We updated the model based on our formativefocus groups with YTM (described below and highlighted in yellow in Figure 1). The barriers to sexual health promotion for YTM that are presented in the pilot data below are now included (highlighted in Figure 1) in the theoretical framework for adapting the MyPEEPS intervention for transmasculine young people.* This framework highlights the role of broader factors including: psychological well-being/emotional regulation, peer and partner relationships, sexual context variables, and stress related to an emerging sexual minority identity (sexual

Figure 1. Social-Personal Framework of HIV and Substance Use Risk



minority stress). *This model guided the development of the content for MyPEEPS Mobile. The model provides clear direction for HIV* prevention programming *related to each of these constructs which are described in Table 3: developing positive peer norms, encouraging associations with non-risk-taking peers and adults, reducing psychological distress, improving emotion regulation, teaching assertive partner communication and safer sex behaviors (e.g., condom use), and developing a healthy personal identity.*

For example, the current MyPEEPS Mobile has content related to sexual minority stress and is presented with 4 ways to manage stigma (see Table 3, activity 17). In MyPEEPS Mobile for YTM, we will update the content to provide information on dealing with stigma specific to YTM and coping with victimization and violence. Guided by this framework, we plan to update the sexual context content to specifically focus on discussions of sexual consent, which was a noteworthy issue amongst the YTM in our focus group sessions. As a final example, our current MyPEEPS

Mobile has extensive information on substance use (see Table 3, activity 7 "Goin' Downhill Fast). For MyPEEPS Mobile for YTM, we will include additional information about the interaction between substance use and gender affirming therapy. Each activity will be reviewed, and we will seek user-informed input from a diverse group of YTM for adaptation as described in the research plan for Aim 1 below.

3.1 STUDY POPULATION

3.2 Inclusion Criteria for All Aims

3.2.1 To participate in any aspect of the study, participants must be: 1) between 15 and 25 years of age; 2) female sex assigned at birth; 3) identify as a transgender man or *along the transmasculine spectrum (including a transmasculine non-binary gender; e.g., male, trans male, transmasculine gender non-binary);* 4) understand and read English; 5) live within the US; 6) own a smartphone; 7) self-report condomless receptive anal or vaginal penile sex with either a cisgender male or transgender woman (e.g., individual designated or assigned male at birth) in the past year; and 8) self-report HIV-negative or unknown status. **Note:** Despite being uncommonly reported in the epidemiological literature on sexual risk among TM, and after careful consideration, we decided to include having had condomless receptive anal or vaginal sex witha transgender woman based on the following considerations: (1) the anatomical mechanics of receptive penile intercourse being the highest risk sexual act for HIV transmission; (2) the high HIV prevalence among transgender women, making that population high risk sexual partners; and (3) our focus groups with YTM reported that penile sex with a transgender woman was not uncommon among the proposed target population. *The eligibility criteria was expanded to include transmasculine gender nonbinary individuals (1) approximately 30% of transgender individuals identify as nonbinary or gender diverse(28), (2) at this age youth identify across the spectrum and are fluid in their identity (3) nonbinary individuals experience similar barriers to healthcare and exclusion from HIV prevention interventions.(29, 30).*

3.2.2 Inclusion of Children

Participants will include children ages 15-17, thus children will be well represented. The investigative team has extensive experience conducting research with youth in the proposed age range. Involvement of children in this study will be in compliance with all applicable subparts of 45 CFR Part 46 as well as other pertinent Federal and State laws/regulations. This project meets standards for inclusion of children.

3.3 Exclusion Criteria for All Aims

Participant exclusion criteria for all Aims. Youth are ineligible to participate in the trial if: 1) they are HIV positive; 2) they are unable to provide informed consent due to severe mental or physical illness or substance intoxication at the time of enrollment; 3) they are concurrently enrolled in another HIV prevention study. **Note:** Given that (a) 72% of our current same-age sample of YMSM age 15-18 reported condomless anal sex in the past year and (b) >800 YTM screened ineligible in our current protocol based on birth-assigned sex alone, but reported considerable behavioral risk, we believe that even with this stringent inclusion/exclusion criteria we will be able to successfully recruit our proposed sample in the timeline proposed. Although these criteria may require us to screen a larger number of participants, we will still be able to reach the recruitment goals, and this is important for assessing the feasibility of this inclusion criteria for a larger R01 trial.

3.4 Recruitment Procedures

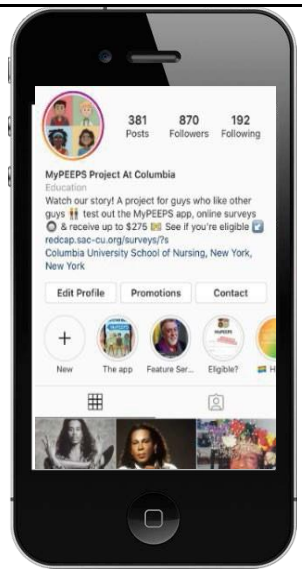
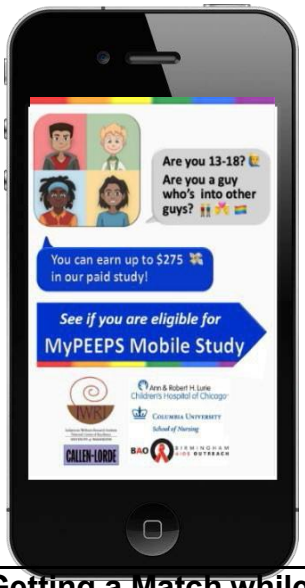
3.4.1 Recruitment Targets

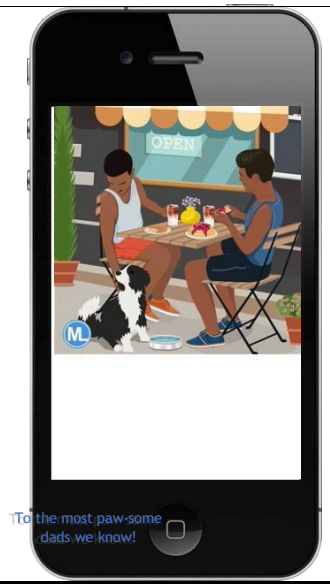
To address all study aims, we will recruit a total of 105 participants. For the heuristic evaluation, we will recruit 5 informaticians. For the usability testing, RCT, and in-depth semi-structured interviews, we will recruit 100high-risk racially diverse YTM in the U.S. using community informed advertisements and messages through electronic methods (e.g., Twitch, Cameo, TikTok, Instagram, Twitter, Facebook, Snapchat partnering with YouTube and Instagram influencers) that we have successfully used to recruit diverse YMSM across several prior NIH-funded projects using social ecological frameworks. We will use these electronic methods to target high HIV prevalence geographic contexts (known as “hot spots”) and EHE jurisdictions. Per the RFA, we will recruit at least 50% of our study participants from the EHE priority jurisdictions. Since 41% of people acquiring HIV annually in the U.S. live outside of EHE priority jurisdictions and are often understudied, we will recruit 50% of our participants from across the broader U.S (non-EHE priority jurisdictions). Additionally, RFA-IA-21-018 calls for research to include 50% racial minorities, which is integrated into our recruitment strategy (30% Black Non-Hispanic and 30% Latinx (all races) YTM). Deliberately including YTM of color is critical, as it is estimated that 50% of Black MSM will acquire HIV in their lifetimes compared to 1 in 11 White MSM.(31)

3.4.2 Targeted Online National Campaign Led by the Study Team

In our own campaigns, we will use race- and age-specific as well as population-based advertising strategies, including psychographic- and geo-targeting (in-depth, publicly available consumer data such as interests; bulk upload by region, city, zip code, or Designated Market Areas (DMA)) to advertise only to potentially eligible individuals. an especially strong following among YMSM. We will also consumer-centered marketing strategies advertise through Twitter, Snapchat, TikTok, Cameo, Twitch and partner with YouTube and Instagram influencers to serve as ‘study ambassadors.’ We will also advertise through popular dating sites (Grindr, Scruff, Grizzly, Hornet, etc.) to recruit study participants who are 18+ years. We will target our recruitment advertising to YMSM of color.(32) Sample ads from our past studies which were developed by our staff with our community-based participants and have been successfully used to recruit Black and Latino YMSM are in **Table 1.**

Table 1. Sample Study Advertisement to Recruit Eligible Participants on Social Media		
a. Instagram Profile	**b. ‘Holding Hands’**	**c. ‘Text Messaging’**

Instagram profile receives on average 1,200 profile visits a week. With 990 followers, interested volunteers visit our active Instagram profile to learn about the study project, watch our story and scroll through content posted daily. In the span of 15 months, the	Featuring two diverse young guys holding hands with a rainbow background, this popular ad was promoted on the feeds and stories of Instagram users using a targeted demographic criterion. In the span of 6 months, 690 eligible volunteers screened	This ad represents the widespread use of text messaging to communicate between adolescent MSM. Over the course of our MyPEEPS RCT, this ad has recruited 338 eligible volunteers of which 63 have successfully enrolled.
study recruited 270 eligible volunteers who screened using the link provided on our profile; 64 of those people enrolled in the MyPEEPS Mobile RCT.	into the study from this ad and 96 have successfully enrolled.	
		
d. 'Paw-some Dads!'	**e. 'Flowers and Laughter'**	**f. 'Getting a Match while at Gym'**

This ad for the mLab App trial features two YMSM sitting outside a coffee shop having breakfast, while one is attending to their dog, the other one is taking a picture of their food for Instagram. This ad affirms the idea that YMSM can in be healthy, happy relationships partaking in activities that in interest them. Our study staff develops relatable LGBTQ study advertisements so potential participants can see themselves represented and know that this study is looking to enroll individuals like them.	Our study staff has developed creatives to represent Black/African American YMSM and highlight the opportunityfor interested volunteers to participate in the mLab App trial, which has been widely advertised across social media platforms as a way to 'participate in LGBTQ research.' Over the years, our study staff has learned that potential participants are very interested in giving back to the LGBTQ community and are looking for ways to activelyhelp in addressing health issuesthat most concern their peers.	In developing ads for social media campaigns, we intentionally combine common interests of YMSM into one impactful image to grab the attention of recruits for the mLab App trial. The ad below depicts a Latino YMSM bench pressing at the gym, whose phone received a notification about a 'match' in an LGBTQ dating app. Although advertising platforms limit targeting to age, gender, and geographic location, our ads showcase real-world behaviors that YMSM are participating in to find eligible men *who are having sex with men*, that is, letting social media users know who we are looking for.
		

3.4.3 Targeted Online National Campaign Led by Commando LLC

Additionally, we will work with our partner, Commando LLC to develop, launch, and execute a national ad campaign. Commando has experience with running successful advertising campaigns and will be working with us to develop social media strategy (including creatives and content such as In-Feed Videos, Reels, Facebook/Instagram Lives, Stories), providing technical support (landing page assistance), and analytics reporting (DMA analysis that provide powerful insights, such as which DMAs have higher conversion rates, engagement, and return on ads spends). They will be advertising on top

LGBTQ dating applications (e.g., Grindr, Growlr, Adam4Adam, Scruff, Jackd,) with whom they've been very successful in reaching YMSM for other studies.

3.4.4 Recruitment Limitations, Anticipated Problems and Alternative Solutions Consistent with

multi-prong approaches designed to reduce recruitment bias, we will employ the aforementioned recruitment methods. We will ward off potential recruitment problems by carefully monitoring each approach to prevent recruitment problems. This will involve weekly review of recruitment data with staff to assess efforts and reports provided by Commando LLC. In this way, the recruitment process will be a dynamic process involving actionable, data-driven insights to help us improve targeting, segmentation, and personalization to improve the recruitment experience for YTM.

3.5 Screening Procedures

3.5.1 Eligibility Screening Procedures

Potential participants will be electronically screened through REDCap(33) for eligibility using the full screening instrument. If a potential participant is screened and eligible and willing to participate, then they will voluntarily provide e-assent/consent. If it is determined during enrollment that a person is concurrently enrolled in another HIV prevention study, they will be deemed ineligible.

3.5.2 Verification of Identity and Initial Screening Criteria

We will use the following procedures to verify the race, sex, and age of participants, and ensure that participants are discrete, not duplicated, and to document the country of residence, for example, individuals living in the U.S. or its territories): 1) Prior to signing the electronic assent/consent form for trial participation, participants are asked to do a confirmatory screening visit via videoconferencing during their baseline phone call to confirm race, sex, and age. If participants become ineligible, we let them know that, unfortunately, we cannot continue with the visit because eligibility has changed; 2) To cross-check age, participants are asked their date of birth; 3) Participants are required to show any form of photo ID during the initial video conference so we can verify identity. If a participant does not have a government or school issued ID, we will ask them to furnish a report card/transcript with their legal name, age, and sex; 4) We will use 2 methods to verify participants' residence: a) We will ask participants to share a form of ID which includes an address, and b) we will cross-check the address on the ID with the IP address that we collect through REDCap software. If there is a discrepancy, we will review with the study participant to better understand if there is a rationale (e.g., participant is in college,). Using procedures previously piloted, we will determine co-enrollment.

3.6 Informed Assent and Consent

At the enrollment visit we will collect written informed e-consent (18 to 25 year olds; assent for 15 to 17 year olds) (see **Appendix A)** for study trial participation, which will detail purpose of trial, study procedures, compensation for contributed time, risks, benefits, site contact information, confidentiality and voluntary participation. The consent process also details the trial and study compensation. YMSM will then be randomized to the intervention arm (MyPEEPS Mobile) or control (delayed intervention) arm.

4.1 STUDY PROCEDURES

4.2 Enrollment Procedures

When a participant screens eligible, a study team member will schedule a visit through a videoconference call using Zoom. These procedures ensure the integrity and success of the study because: 1) We are able to eliminate fraud by verifying participants' identities via videoconference, fraud being a potential problem in online research,(34, 35) and 2) We establish rapport with our study participants and have seen very high retention rates related to this rapport building between our staff and study participants, which will be augmented by electronic retention strategies in this study.

4.3 Locator Form/Contact Information

At enrollment, participants will be asked to provide contact information to contact them throughout the duration of study for follow-up assessments. This information will be captured in REDCap may be updated during follow-up assessment and/or whenever the participant needs to update their contact information on file. We will collect each participant's cell phone number, email address, as well as encourage them to share their social media handles (e.g., Snapchat, Instagram, Twitter Facebook, WhatsApp, and/or Skype usernames). Participants will be asked if it is okay to mention the name of the project and method(s) of study communication preferred when receiving automated reminders (e.g., text messaging, email, phone call, leave voicemail). Study staff will not send messages or leave voicemail messages unless expressly permitted to do so by the participant. If permission is given to leave voice messages, site staff will assure participants that messages left will not include any protected health information or information related to study participation. If permission is given to send text messages and/or if study staff is unable to get in contact through email, staff will send text messages using an IRB-approved messaging script to contact participants throughout the duration of the study. Contact information will be maintained using the same confidential data management practices used for all study data.

4.4 Specific Aim 1 Procedures.

Specific Aim 1: Using qualitative methodology, expert feedback, and usability assessments, develop MyPEEPS Mobile for YTM.

MyPEEPS was built on considerable formative work with multi-racial and ethnic groups (R34MH079707; PI: Garofalo and U01MD011279; MPIs: Schnall and Garofalo). Findings from the U01 have been peer-reviewed and published.(27, 36-40) In preparation for this R34, we conducted extensive preliminary work to identify the common themes, concerns, and HIV risk and protective factors in YTM to expand MyPEEPS and ensure its acceptability for this group*, particularly for YTM who are multi-racial or come from communities of color*. *This will be done* using the focus group data collected from 49 YTM in our preliminary work for this application, and through the feedback by our Expert Review Panel and usability testing with YTM.

Expert Review Panel. The goal of this panel is to reach censuses on common concerns, risk, and protective factors for YTM.

Procedures. The expert and youth advisory panels provided feedback remotely by reviewing the curriculum and providing written comments.

Development of mobile delivery technology. Following the expert panel sessions and building on our findings from our formative focus groups, we will develop mock-ups of a MyPEEPS Mobile App with our

partners at One Cow Standing, a software development company (see Letter of Support). The mockup will have partial functionality of the system and enable us to test the design. MyPEEPS Mobile for YTM will be novel, innovative, scientifically sound, scalable, translatable, and likely to have a strong public health impact, as detailed in the Innovation section. Dr. Radix will oversee all updates to the content of the MyPEEPS Mobile App, with support from MPIs Drs.
Schnall and Garofalo. *The final product of this work will be a Beta version of the app for usability testing.*
Refinement of the MyPEEPS Mobile. Following the development of MyPEEPS Mobile for YTM, we will conduct usability testing. **Usability Testing.** The goal of usability testing is to improve the design and increase the likelihood of technology acceptance. We will evaluate the user interface and system functions of the MyPEEPS Mobile App and assess whether they are consistent with the end-users' needs. We will conduct two types of usability assessments: A) **Heuristic Evaluation** and B) **End-User Usability Testing**.

Heuristic Evaluation. Sample: Five informaticians with training in human-computer interaction and who have published in the field of informatics will be recruited as usability experts. Nielsen recommends using three to five evaluators since one gains little additional information by using larger numbers(41). We will recruit them through direct contact with the Informatics Departments at Columbia University and Weill Cornell Medical College, both of which have a large cadre of informatics researchers. Dr. Schnall will send a message to potential evaluators via email using the MyPEEPS Heuristic Email Recruitment Script. Procedures: The heuristic evaluator will be consented using the Heuristic Evaluation Consent form. Once consented,the heuristic evaluators will assess a web-based Beta version of the MyPEEPS Mobile App remotely via Zoom software. Evaluator screen movements and audio will be recorded via Zoom. Identifiable characteristics, such as facial features and names, will not be recorded. Similar to procedures that we have used in ourprior work(42-44), each evaluator will be asked to evaluate the system using the Heuristic Evaluation Checklist and to think-aloud while performing the usability testing(45). Participants will be asked to say aloud what they are thinking, seeing, and trying to do while they are performing the tasks required for the scenarios. When a user finds errors or the researchers find critical incidents that are characterized by comments, silence, or looks of puzzlement, the researcher will record the users' activities.
Recording the users' interactions and vocalizations provides additional feedback that can highlight problems that would not be identified with static screen shots(46). Each evaluator will walk through the use case scenarios (see "MyPEEPS Heuristic UseCaseScenarios Procedure 11.16") and a study team member will navigate through the app per evaluator instructions to complete the assigned tasks. Once the walkthrough is complete, the evaluator will fill out the Qualtrics survey titled, "Heuristic Evaluation Survey." After the heuristic evaluation, participants will be asked to rate the prototype's perceived ease of use and perceived potential usefulness using a standardized instrument. Instrument: Nielsen(47) proposed a list of ten recommended heuristics for a usable interface design. Each heuristic will be evaluated by one or more items, and the overall severity of the identified heuristic violations will be rated.(48) Evaluators will also complete the Health Information Technology (IT) Usability Evaluation Scale (Health-ITUES) to rate usability. This tool varies from most traditional measurement scales in that it is designed to support customization at the item level to match the specific task/expectation and health IT system while retaining standardization at the construct level. The Health-ITUES supports evaluation of three levels of task/expectation: user-system, user-system-task, and user-system- taskenvironment. Schnall (MPI) has published on the usefulness of the Health-ITUES for evaluating the usability of mHealth technology(53). Data Analysis: The frequencies of usability issues will be calculated according to the heuristic principles adapted from Nielsen's checklist.
Mean severity scores will be calculated for each heuristic principle. Evaluators' comments about usability

problems on the evaluation form and the recording will be grouped and content analyzed according to the usability factors of Nielsen's heuristics.(49) Recordings will be kept until data analysis is complete and findings have been disseminated. Heuristic evaluators will be compensated a $150 Amazon gift code for their time and will receive the gift code via email using the Heuristic Evaluator / Usability Compensation Email Template.

Usability Testing with YTM. We will conduct usability testing with YTM to identify violations of usability principles and any potential obstacles to their effective use and content of intervention adaptation of MyPEEPS Mobile with members of our advisory board of transmasculine youth. This is an iterative process that involves testing the system and then using the results to change it to better meet users' needs. Sample: We will recruit 20 YTM (15-25 years old) who will participate remotely in the formative evaluation of the prototype user interface screens. The rationale for 20 participants is based on past usability research, which has indicated that 95% of usability problems can be identified with 20 users(50). These youth will serve as community voices, specifically youth as advisors. We will purposely sample our usability testing participants to ensure diversity regarding race, ethnicity, and age. We will be recruiting by reaching out to participants in our REDCap database who previously expressed interest in the study or participants who are enrolled in another one of our studies. When we reach out to these participants in REDCap, we will be using the MyPEEPS Participant Outreach Script. We will also be using flyers for recruitment, once approved by the IRB. Participants will be screened for eligibility using the Usability Screener in REDCap. Procedures: We are requesting a waiver of documentation of consent for online screening procedures. The screening information will only be kept electronically in REDCap, which is a secure, CUMC approved system. If participants screen eligible, study staff will go through the informed consent process with participants. If participants consent to participate, they will complete the Assent/Consent form for Usability Testing. Participants will complete a brief demographic background and computer usage survey.

Participants will use a web-based beta version of the MyPEEPS Mobile with screen movements and audio recorded via Zoom software. Identifiable characteristics, such as facial features and names, will not be recorded. After the usability evaluation, participants will be asked to rate the prototype's perceived ease of use and perceived potential usefulness using a standardized instrument. Instrument: We will measure self-reported ease of use and usability with the Health Information Technology (IT) Usability Evaluation Scale (Health-ITUES)(51, 52). Data Analysis: The analysis will be based on the recordings of user sessions, transcriptions, notes, and the user surveys, and mean task performance time will be calculated. Dr. Schnall will search for critical incidents which will be characterized by comments, silence, and repetitive actions. Dr. Schnall will review these incidents in detail using Zoom software. The incidents will be identified, and the users' written comments summarized. Content analysis, a technique for making replicative and valid inferences from data, will be performed by the research assistant under Schnall's supervision. The comments will be categorized according to the positive characteristics, negative characteristics, and recommendations made by the end- users. Results from the standardized surveys will be analyzed using SAS 9.4 (SAS Institute, Cary NC) to calculate the descriptive statistics to complement the findings from the usability assessment. Using the findings from these activities, we will refine MyPEEPS for use in Aim 2. Recordings will be kept until data analysis is complete and findings have been disseminated. Participants will be compensated for their time in the form of a $40 Amazon gift code and will receive the gift code via email using the Heuristic Evaluator / Usability Compensation Email Template.

4.5 Specific Aim 2 Procedures.

Specific Aim 2: Conduct a pilot randomized controlled trial to examine the feasibility, acceptability, and preliminary efficacy of the MyPEEPS Mobile App for YTM in a sample of 80 YTM (15-25 years) and refine the study methods for a future efficacy trial.

Overview. We will conduct a 6-month randomized controlled pilot study with 80 YTM. The goals of the pilot study are to: a) Gain direct feedback from participants about whether and to what degree the MyPEEPS Mobile App worked as intended; b) Assess the acceptability of MyPEEPS Mobile dosing and content for YTM; and c) Observe the flow of procedures, including assessment at baseline, retention efforts, data management, and follow-up assessments. The recruitment plan, screening, and consent/assent processes are described in the Protection of Human Subjects and Clinical Trials Information sections. Our **primary outcome for this study will be:** change in number of condomless receptive anal or vaginal sex acts with *sex partners assigned* male *at birth*. **Sampling Approach to Successfully Enroll YTM in this Project.** We will recruit 80 participants from an online national sample and ensure that at least half of our sample is from racial/ethnic minority groups. Using active and passive recruitment methods, the on-site project coordinators will oversee and participate in recruitment efforts. The study staff hired for this project, on-site coordinator, and the peer-to-peer networking efforts will be used to recruit study participants. Our pilot study will comprise a convenience sample through active online recruitment through Instagram, Twitter, Snapchat, and Facebook advertisements. We will use psychographic targeting (in-depth, publicly available consumer data such as interests, city) to advertise only to potentially eligible individuals. We have successfully used this approach to recruit our sample of YMSM in the MyPEEPS project. Through our advertisements, and as previously mentioned, we have screened
>800 YTM who would be eligible for the proposed MyPEEPS study, *and we will plan to recruit them as well as others into the proposed study. We are confident in our ability to enroll the proposed target sample*.

Sample Size and Power Calculation. This study plan is to enroll 80 participants with 1:1 random assignment to the intervention arm and the control arm (i.e., 40 in each arm). Compared to a large-scale randomized trial, we do not expect that this pilot trial will have power to detect many of the

effects that would be of scientific or have policy significance. This is consistent with the aims of this pilot grant mechanism, where budgetary limitations necessitate small sample sizes. Group means on continuous variables typically begin to stabilize by 20-30 subjects. Thus, a sample size of 40 participants per group should provide relatively stable group means for the intervention and control conditions, even with some sample attrition.

Potential Problems/Alternative Solutions Regarding Recruitment. Consistent with the multi-prong recruitment approach designed to reduce recruitment bias(54, 55), our team will carefully monitor each approach to prevent recruitment problems. This will involve weekly review of recruitment data with staff to assess efforts. In this way, recruitment will be a dynamic process and will reach the proposed diverse group of YTM.

Eligibility Screening and Informed Assent/Consent. See Protection of Human Subjects.

Study Enrollment. A baseline visit will be conducted involving a behavioral assessment and will last approximately 1.5-2 hours. YTM will then be randomized to the intervention or delayed intervention arm. An enrollment project will be created in REDCap to collect and manage data for enrolled participants. The longitudinal study module, automatic survey invitations, and secure file upload capabilities can be used in conjunction with customizable reports to ensure streamlined operations and efficient data management. Eligible volunteers will be scheduled for a one-time

face-to-face video call (e.g., Zoom), with a study team member to enroll. The enrollment visit is conducted via video to validate identification and age (view identification documents) and build rapport to support retention over time. Study staff will create a record for the volunteer, and REDCap will send the volunteer a customized interview assessment via e-mail beginning with the consent/assent process with electronic signature capability. The longitudinal module of REDCap will automate follow-up data collection by generating a unique study visit schedule for every participant, anchored to their enrollment date. Paired with automated survey invitations, participants will be automatically invited via e-mail to complete follow-up surveys based on their unique study visit schedule. These invitations include up to 5 automated reminders sent in pre-defined intervals. Staff monitor the completion of follow-up survey data at 3 and 6 months, which include the primary and secondary outcome assessments, via the reports, which query the completion status in real time.

Table 3. Overview of MyPEEPS Content and Activity Type

Module Number/Name/Screenshot from App Module	Activity Number & Name	Activity Content	Activity Type
Module 1. Introduction	1. Welcome to MyPEEPS	User inputs name, telephone number, e-mail address, and how they prefer to get notifications.	Questions
	2. BottomLine	User is asked the furthest they will go with a one-time hookup in several sexual scenarios.	Multiple Choice
	3. Underwear Personality Quiz	User completes personality quiz and is introduced to characters in the app.	Multiple Choice
	4. My Bulls-I	User is asked to input the ways they refer to their body parts after seeing an example from one of the app characters.	Open-Ended Questions

Module 2. Serious Talk 	5. P's On-Again, Off-Again BottomLine	Video animation of text messaging conversation between two characters, P and Nico, about P's new relationship that has led him to ignore his BottomLine. The user is asked to complete questions about why P should be concerned about his BottomLine.	Video and Multiple Choice
	6. Sexy Settings	User is presented several settings in which sex takes place and potential threats to BottomLine and asked to match each setting to correct threat.	Matching
	7. Going Downhill Fast	User is presented with information about effects of alcohol and common illicit or misused drugs. Resources for additional information on each substance are provided via external web links. After reading through information, users match substances to potential threats.	Matching
8. Move Up, Move Back	User is asked series of questions related to their own life experience. User is introduced to personal identities and characteristics that may place them at a societal advantage or disadvantage, termed "VIP (privileged)/General admission (non-privileged)" status		Yes/No Questions
9. HIV True/False	User completes a series of True/False questions related to HIV, with detailed fact-based information provided for each response.		True/False
10. Jeopar-T	User completes a series of True/False questions related to hormones, reproductive health, and surgeries to win points.		True/False
11. Checking In On Your BottomLine	User is given opportunity to review and make changes to their BottomLine, taking into consideration any information they learned from completed activities.		Multiple Choice
Module 3. Safety First	12. P Learns About Safer Sex	User is presented with a scenario about P trying to make his way to clinic for HIV testing on public transportation. P experiences difficulties and rude behavior on the bus and user is presented with recommendations for managing anger and frustration.	Video
	13. Tackling Testing	User watches a video animation about what to expect during Tommy's first experience being tested for HIV and P's experience seeking testing and reproductive healthcare. Video presents clinic scenario and discussion with a health provider.	Video

	14. Spread Out	User completes an activity matching a given sexual act with its corresponding level of risk (no risk, low, medium, high), to apply lessons learned in prior activities specific to HIV/STI transmission risk.	Matching
	15. Steps to	User is presented with 12 steps for effective condom use and must correctly	Ordering Question

	Effective Condom Use	order the steps by selecting them sequentially from list of all steps.	
16. Safer Injection	User is given the opportunity to review the safe needle injection steps. User then completes an activity matching safer injection steps to images.		Matching
17. Checking In On Your Bottom Line Again	User is again given the opportunity to review and make changes to their BottomLine, taking into consideration any information learned in prior activities.		Multiple Choice
Module 4. Making Tough Situations Safer	18. Disclosure and Safety	User is presented with emotional coping strategies to manage disclosure and responses from potential partners while dating.	Multiple Choice
	19. Red Flag, Green Flag	User is presented with dating app profiles and learn about online safety as they decide whether or not they would engage the profile further.	Yes/No Questions
	20. Peep in Love	User is presented scene where P is confronted with a “swirl of emotions” related to a sexual encounter and presented with management techniques to stick to their BottomLine.	Multiple Choice
	21.Healthy Relationships	User is presented with a dating scenario between two characters. They are asked to identify characteristics of the relationship as healthy or unhealthy.	
	22. 4 Ways to Manage Stigma	User is presented with four different strategies to manage stigma. They are then asked to match those strategies to scenarios presented as comic panels.	Matching
	23. Get a Clue!	User is presented with a “slot machine” activity in which combinations of feelings, partner characteristics, and settings are presented, and they are asked what sexual decision they would make in each scenario, keeping their BottomLine and communication strategies in mind.	Multiple Choice
	24. Last Time Checking In On Your Bottom Line	User is given final opportunity to review and make changes to their BottomLine, taking into consideration any information learned from completing prior activities	Multiple Choice

	25. BottomLine Overview	User is presented with chronology of how their BottomLine changed throughout the app and encouraged to continue to stick to their goals for sexual safety.	Summary

Randomization to Intervention and Control (Delayed Intervention) Arms. Using the randomization module in REDCap and the approach described below, there will be random or minimally biased assignment of subjects to study arms. We will use block randomization with randomly permutated blocks(56) to reduce opportunities for selection bias. The advantage of the permutated block design is that treatment assignment is pre-determined before the trial begins and then assignment remains static throughout the course of the trial(57). Blinding and random assignment will be maintained through continuous supervision by key members of the research team. All staff and participants will be kept blinded to outcome measurements during data collection(58). This technique will maintain complete randomness of the assignment of a subject to a group. Participants will be randomized based on the use of a password protected computer- generated random numbers at baseline to avoid the possibility of study staff subverting randomization as has been noted in previous studies(59). Following completion of the informed assent/consent and baseline assessment, participants will be randomly assigned to one of the two trial arms using the randomization module in REDCap(57). This willminimize the biased assignment of study subjects(60).

Intervention Delivery. If the study participant is randomized to the intervention arm, they will have access to the MyPEEPS Mobile App for the next three months. Participants randomized to the control (delayed intervention) arm will be given access to MyPEEPS Mobile at the 3-month study visit. Through our dashboard, we can monitor when participants login to MyPEEPS Mobile, time spent on each activity, and whether they are actively using the intervention or just logged in. Participants will have 3 months to complete the 4 MyPEEPS Mobile modules, which includes 25 embedded mobile activities (See **Table 3**).

Participants in the intervention group will be able to access the MyPEEPS intervention from baseline until the end of month 3 and the control arm (delayed intervention) will have access to the MyPEEPS App from months 4-6 (see **Figure 2**). **Overview of data collection time points.** We will conduct simultaneous assessments for both study arms at baseline, 3 months, and 6 months. The delayed intervention design is essentially a cross-over design in which data are collected in parallel from both study arms through the primary endpoint - 3-months post-randomization (**Figure 2**). The arms are then crossed over, which has multiple benefits, including: 1) for ethical reasons per our experience with HIV prevention interventions with transgender populations, the delayed intervention group receives the potential benefit of the

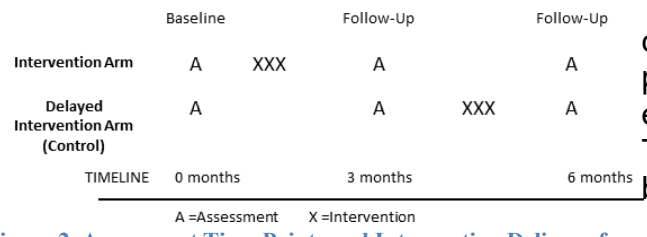


Figure 2. Assessment Time Points and Intervention Delivery for Each Study Arm

intervention at the point of cross-over; 2) at the 6-month follow-up, it provides for a test of the durability of the intervention effect in the intervention group (i.e., 3-months post-intervention, pre-post); 3) it provides an additional secondary test of the intervention effect in the delayed intervention arm (pre-post); and 4) it provides additional time points (and power) in the intervention group to test moderators of the trajectory of sexual risk over time. We successfully used this study design in an NIH-funded R34 study(61).

MyPEEPS avatars represent "regular guys" like the study participants who will walk the participants through the curriculum. Following the selection of an avatar, the study participant will navigate through each of the study activities. Participants do not need to complete an activity in a single sitting but can stop and come back to complete the activities at any time during the time frame before the 3-month follow-up. Study staff will have access to a dashboard to monitor module completion. In addition, participants will receive weekly text messages and/or e-mails (participants will select) to remind them to complete the MyPEEPS module. If 2 weeks have passed and a participant has not completed any modules, then the app will send out notification reminders to remind them to complete their modules.

4.6 Specific Aim 3 Procedures.

Overview. Post-intervention, we will conduct individual, in-depth, semi-structured interviews with participants who completed the intervention.

Sample. We will purposively select participants to represent a diverse set of experiences (e.g., participants who completed App Use, high vs. low sexual activity). Although we will continue to recruit participants until reaching thematic saturation, we anticipate conducting about 20 interviews

Procedures. The in-depth interviews will be 45-60 minutes in length. Following completion of the informed consent process, all interviews will be audio-recorded. The interview guide will be informed by the predisposing, reinforcing, and Enabling Constructs in Evaluation (PRECEDE) portion of the PRECEDE-PROCEED Model of health program planning and evaluation(62). In addition to the evaluation of public health programs, this framework has been applied to the evaluation of health information technology and has been proposed by several authors as a strategy for assessing predisposing, enabling, and reinforcing factors for use and acceptance of health information technology tools(63-65). Structured interview questions are listed in Table 4.

Table 4. Structure Interview Guide

1) What are your experiences with accessing HIV prevention information? Describe your experience finding information relevant to YTM. How does this information compare to the information in the MyPEEPS App?
2) What was your experience using the MyPEEPS App and how did it affect your decisions about your sexual behaviors?
3) What were some of the barriers to using the App? Incorporating the content into your daily life? (predisposing factors)
4) What are your ideas about strategies for overcoming these barriers? (enabling factors)
5) What are some of the ways that your overall health might benefit from the MyPEEPS App? (reinforcing factors)

Ensuring Rigor. The team will adhere to qualitative research processes to ensure the credibility, confirmability, dependability, and transferability of the qualitative data from these analyses.(66) To support the credibility of the data, we will conduct peer debriefing and triangulate findings across multiple data sources (surveys, interview data). In addition, we will use "member checks," i.e., sharing of initial data interpretations with participants to ensure accurate interpretations. Triangulation of findings, along with reflexivity, will enhance the confirmability of the interpretations. The investigators will carefully record an audit trail and keep extensive field notes to facilitate transferability of study findings into other contexts. Table

Data Analysis. All in-depth interviews will be transcribed verbatim and then coded. Recordings will be kept until data analysis is complete and findings have been disseminated. The development and application of a coding scheme is an integral component of the data analysis process. It enables the systematic examination and interpretation of the data related to the primary analytic foci. The coding scheme is conceptualized as a multilevel structure. At the highest level are the primary analytic foci coded as headings. Specific aspects or dimensions of the headings are assigned core codes. Specific aspects or dimensions of the core codes are assigned sub-codes. We will use NVivo™ (QSR International, Victoria, Australia), a software program for qualitative analysis, to facilitate the analysis. The following 7 steps will be used to develop the coding scheme: Step 1: Identify the principal issues discussed by participants; Step 2: Construct definitions of the primary analytic themes; Step 3: Develop and apply core codes and sub-codes to the initial set of interviews; Step 4: Develop a provisional coding scheme; Step 5: Test and refine the provisional coding scheme; Step 6: Reconcile coding differences and construct an updated and final coding scheme; Step 7: Apply the coding scheme to the full data set and assess inter-coder reliability. After all transcripts have been coded, we will extract and examine the content of text segments linked to core codes and sub- codes relevant to understanding barriers and facilitators to the use of the MyPEEPS App. Based on the coded data, we will propose ways in which certain themes are analytically related. A careful examination of the coded text will reveal the associations among these themes and may lead to more refined data searches. Once we establish patterns of relationships among themes and issues, we will identify participants' accounts that support or refute these patterns. Identifying and accounting for cases that deviate from an interpretative pattern enables us to test and confirm the pattern's validity and robustness.

Triangulation of Findings. We will examine changes in HIV risk behaviors and its relationship to factors including but not limited to changes in substance use, alcohol use, stigma, victimization. We will triangulate the findings from our quantitative outcome measures (Aim 2) with the findings from our qualitative data (Aim 3) to better understand participants' decisions for their HIV risk behaviors.

Anticipated Problems and Alternative Study Design Considerations. The study team thought very carefully about alternative design considerations. (1) We carefully considered a more traditional RCT design and control group. However, in prior HIV prevention interventions projects targeting transgender populations we received considerable negative pushback from the community regarding this approach(67). (2) We carefully considered less stringent sexual risk inclusion criteria, but firmly believe that we can recruit the proposed sample using condomless sex as our outcome variable. (3) If needed for recruitment to maximize participants who report condomless sex, we can expand the age range to 25 years based on age range of the original MyPEEPS trial.

Summary. The final product of this study will be the basis for an R01 application to conduct a large-scale efficacy study for this population. The proposed MyPEEPS Mobile intervention for YTM is a novel and evidence-driven intervention using mobile technology to deliver HIV

prevention information specifically developed for YTM. Consequently, we are confident that proposed intervention will be of high impact intervention for improving HIV prevention behaviors in YTM and have long-term implications for overall improvement in the public's health.

5.1 DATA COLLECTION AND SITE MONITORING

5.2 Development of Protocol and Case Report Forms

The Protocol Team in collaboration 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.

5.3 Data Records

Participant-related study information will be identified through a Participant ID (PID) on all participant CRF and Computer Assisted Self Interviewing (CASI) files. Participant names or other personally-identifying information will not be used on any study documents and will be redacted from interview transcripts. Participant names and their PID will be stored separately from other study information in REDCap or secure University servers, accessible only to designated study staff, site monitors, and representatives from the NIH. PIDs will not be entered into the MyPEEPS Mobile app; instead, a unique username will be assigned to each participant when they create an account for the MyPEEPS Mobile app. These unique usernames will be provided by the study team. Original source documents for individual participants will be maintained at the respective study site and will be accessible only to the study staff. Data from original source documents will be transcribed on CRFs as applicable.

5.4 Data Collection

5.4.1 CASI Data

Data collected using a web-based CASI method will be on a portable computer, tablet, or mobile phone (what the participant chooses) via an internet-based application. All survey data will be collected using REDCap. Data will remain confidential. The participant's unique PID # will be used in order to link the responses to the participant.

5.4.2 Zoom Platform Description

Zoom will be used to schedule videoconference with participants remotely for screening and enrollment procedures. Zoom is compatible on PCs, tablets, and smartphones; as well as maintains the option to conduct an audio conference without the video component. Zoom is 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).

5.4 Data Submission

5.4.1 CASI Data Transmission

Only authorized users will be able to access and open the survey through REDCap. To ensure data privacy, as soon as data is entered (in real-time), it will be encrypted during transmission to REDCap. The data will routinely be downloaded and stored in a secure database on University servers.

5.4.2 Retention Data

The study will use a Health Insurance Portability and Accountability Act (HIPAA)-compliant web-based platform entitled REDCap, which aids 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. REDCap provides study staff the ability to conduct data entry for longitudinal participant tracking from screening to study completion and to use secure messaging, study calendar management, secure photo uploads. The ability to designate specific roles with certain levels of access to every REDCap user 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.

5.5 Data Quality Control and Quality Assurance

Investigators receiving federal funding must adhere to the Code of Federal Regulations (CFR) to protect research participants and produce reliable study information. The study coordinators will monitor data entry and will have an internal quality assurance plan that will identify problems and correct errors in research study records.

5.6 Study Site Monitoring and Record Availability

Site monitors under contract to the National Institute of Allergy and Infectious Diseases (NIAID) will visit participating clinical research sites to review participants records, including consent forms, CRFs, medical records (e.g., physicians' progress notes, nurses' notes, individuals' hospital charts), and laboratory records to ensure protection of study participants, compliance with the IRB approved protocol/amendments, and accuracy and completeness of records. The monitors will inspect sites' regulatory files to ensure that local regulatory requirements, in addition to U.S. Federal regulations, are being followed. They will also inspect sites' pharmacies to review product storage and management.

6.1 PARTICIPANT TRACKING & CLINICAL MANAGEMNT

6.2 Retention Efforts

Study staff will track retention, which will be reviewed weekly by the PIs. As has been successful in previous studies with this population, including the MyPEEPS Mobile efficacy trial, we will: 1) obtain, at baseline, participants' email addresses, phone numbers, social media handles, as well as the addresses and contact information of people participants believe could help us locate them in the future; 2) allow for any time of day, and all days of the week, for participants to complete online assessment visits; 3) provide participants with numerous methods for contacting study staff, including providing study phone numbers, email addresses, and social media handles and if agreed to by the participant, having them program our site numbers into their mobile phone during the enrollment visit; 4) routinely verify participants' locator information at every contact point; 5) if correspondence is returned indicating a participant no longer has a given email address, study staff will telephone to obtain their new email address; 6) if the phone number is disconnected, we will contact them via their social media accounts and/or individuals listed in participants' records; and 7) if participants are not responsive after 5 email correspondence attempts and/or have given permission to message them via phone number, we will attempt to make contact using participants' phone numbers using IRB-approved scripts. We will make every effort to maintain contact with participants, even if they move or discontinue the intervention, for those still willing to complete follow-up assessment visits. Given the older study population proposed in this trial, we are confident we will retain at least 80% of the study population for this study proposed in this trial, we are confident we will retain at least 80% of the study population for this study.

6.3 Intervening on "Social Harm"

All sites have specific policies governing the treatment of human participants. 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. 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 or her safety. Reporting will be done as appropriate to the situation and the legal statutes, including reporting to child protection agencies or other appropriate agencies and referrals will be provided to appropriate support, counseling, or treatment resources.

6.4 Criteria for Permanent Intervention Discontinuation for an Individual Participant

The criteria for permanent discontinuation of further study intervention for an individual participant are:

- Study product/intervention-related adverse event
- Reaching a defined clinical endpoint
- Completion of study intervention as defined in the protocol
- Request by participant to terminate study intervention
- Clinical conditions, which in the best judgment of the investigator are believed to be harmful or potentially life-threatening to the participant, even if not addressed in the AE Management section of the protocol

Participants may end their participation in the study at any time. No further data collection will occur from the date the decision is made to permanently discontinue the subject from the study. Participants who experience distress during the survey can access our list of community referrals, which can be viewed on our study's website, or contact the research staff using the information provided to the participant within the consent/assent process. Any unexpected adverse events will be immediately reported to the Columbia University IRB, if applicable. All study activities will halt pending Columbia University IRB review and recommendations if necessary. If a participant withdraws or is removed from the study, the site study coordinator will complete the necessary documentation regarding the participants off study status.

6.5 Criteria for Premature Study Discontinuation for an Individual Participant

The criteria for premature discontinuation from the study for an individual participant are:

- Lost to follow up as evidenced by failure by the participant to attend specified consecutive clinic visits, at the discretion of the site investigator;
- Participant repeatedly non-compliant with study intervention as prescribed;
- Request by participant to withdraw assent/consent;
- The study is cancelled by the NIH;
- The study is cancelled for other administrative reasons;

- The participant becomes incarcerated or placed in detention during thestudy;
- The participant reports an HIV positive diagnoses;
- Participant judged by the investigator to be at significant risk of failing to comply with the provisions of the protocol as to cause harm to self or seriously interfere with the validity of study results; or
- Death of the participant

7.1 DATA MANGEMENT, SECURITY & ANALYSIS

7.2 Power Considerations and Sample Size Calculation (Aim2)

Sample Size and Power Calculation. The study plan is to enroll 80 participants with 1:1 random assignment to the intervention arm and the control arm (i.e., 40 in each arm). Compared to a large- scale randomized trial, we do not expect that this pilot trial will have power to detect many of the effects that would be of scientific or policy significance. This is consistent with the aims of this pilot grant mechanism, where budgetary limitations necessitate small sample sizes. Group means on continuous variables typically begin to stabilize by 20-30 participants. Thus, a sample size of 40 participants per group should provide relatively stable group means for the intervention and control conditions, even with some sample attrition.

Study Design. Participants in the intervention group will be able to access the MyPEEPS intervention from baseline until the end of month 3, and the control arm (delayed intervention) will have access to the MyPEEPS App from months 4-6.

Overview of Data Collection Time Points. We will conduct simultaneous assessments for both study arms at baseline, 3 months, and 6 months. We will also collect an immediate post-intervention assessment for the delayed intervention arm. The delayed intervention design is essentially a cross-over design in which data are collected in parallel from both study arms through the primary endpoint - 3 months post-randomization. The arms are then crossed over, which has multiple benefits, including: 1) for ethical reasons per our experience with transgender populations, the delayed intervention group receives the potential benefit of the intervention at the point of cross-over; 2) at the 6-month follow-up, it provides for a test of the durability of the intervention effect in the intervention group (i.e., 3 months post-intervention, pre-post); 3) it provides an additional secondary test of the intervention effect in the delayed intervention arm (pre-post); and
4) it provides additional time points (and power) in the intervention group, to test moderators of the trajectory of sexual risk over time.

7.3 Data and Safety Monitoring

7.3.1 Training on Human Subjects and Data Safety and Monitoring.

All proposed staff have participated in the NIH required trainings for conduct of studies that involve human subjects and any future study staff will do so upon hiring. Training for all staff

includes (but is not limited to) Protection of Human Subjects, Informed Consent, Good Clinical Practice, Quality Management, Confidentiality, and Reporting of Adverse Events, REDCap data entry and management. If any study staff discovers any untreated condition (e.g., onset of physical or mental health condition), they will refer participants to appropriate treatment immediately.

7.3.2 Data Management and Data Quality

Columbia University will be responsible for computerized survey programming, data capture, management, and analysis. All study information will be identified through the Participant Identification Number (PID) on all forms and computerized files. Data files will be exported from the ACASI program and imported into the SPSS database for storage. Computer data files never have any identifying information and are encrypted prior to transfer between study sites. Data entered into the SPSS database will not include any identifying information. Only authorized users with a login name and password will be able to open the computerized survey, and only those with administrative privileges will be able to access data. The study research assistant (RA) will use a login name and password to gain access to the software to administer it to a participant, but they will have no ability to access the saved data. The database, data structure, and data quality will be routinely reviewed by Dr. Schnall, and the Data Manager will set up the database, check data quality, and prepare the data for use. The Multiple PIs will work closely to plan analyses for various purposes, including for hypothesis testing and manuscript development and reports. Data quality will be examined before statistical analyses are conducted, including examination of missing data,

assessment of distributional assumptions, and identification of outliers. In addition to data quality, the comparability between intervention and control groups will be carefully examined, including baseline balance and differential attritions at all waves of follow-up. While differences are not expected from the randomized design, it is prudent to plan for this contingency so that sufficient follow-up data and appropriate statistical methods can be used for intent-to-treat analyses. The psychometric properties of instruments will also be examined, as will the patterns of missing data.

7.3.3 Data Monitoring

For the study, weekly reports for the sites will be created by the data manager to review relevant app engagement data, barriers with recruitment/enrollment and retention, urine sample collection, compliance with the protocol, and accuracy and completeness of the records. The investigative team will hold reoccurring conference calls, and these reports will be briefly reviewed by the team at these meetings. These regular reviews will ensure close communication between the research assistants, quickly identify missing data points, and ensure consistent management of any issues with the protocol between sites.

Data quality will be examined before statistical analyses are conducted, including examination of missing data, assessment of distributional assumptions, and identification of outliers. In addition to data quality, the comparability between intervention and control groups will be carefully examined, including baseline balance and differential attritions at all waves of follow-up. While differences are not expected from the randomized design, it is prudent to plan for this

contingency so that sufficient follow-up data and appropriate statistical methods can be used for intent-to-treat analyses.

7.3.4 Data Safety and Monitoring Board

The contact Principal Investigator (PI) will enlist a Data and Safety Monitoring Board (DSMB) to oversee the data, safety elements, and overall integrity of the study. The DSMB will: 1) monitor recruitment, enrollment, and adherence of study participants; 2) formulate criteria for modifying or discontinuing the intervention of individual subjects; and 3) review serious adverse events (SAEs). The objectives of the DSMB will be to assess the safety of the intervention trial and to assure the highest degree of subject safety. We will work with the NIMH to identify individuals to serve in this role. Monitoring board membership will be reviewed and approved by NIMH. Should there be any questions regarding the independence of the monitoring board it will be addressed and corrected if necessary.

The biostatistician with clinical trials expertise and the data manager will prepare monitoring reports in advance of every DSMB meeting. The DSMB will remain blinded to randomization status unless, for safety reasons, the DSMB, in consultation with the NIMH Program Administrator, decides it is important to unmask the data.

The DSMB will: 1) review the protocol as funded and make suggestions for any changes (especially safety related); 2) assess the endpoints suggested by the investigators; 3) review study progress by reviewing recruitment, retention, and compliance of participants and data quality; 4) determine formatting for data reports; 5) review endpoints for safety; 6) submit written reports and

suggestions to the team; and 7) add to or modify this list of objectives. The Project Director will document the minutes of the meetings and distribute to the Chair of the DSMB for final approval or revision.

7.4 Adverse events

7.4.1 Adverse event assessment

We anticipate that the Data Safety and Monitoring Board will define study-specific serious adverse events (SAE)s. While we do not anticipate any SAEs, we will suggest looking for imbalance among treatment arms with regard to the following criteria: safety and data security and study drop-out

7.4.2 Adverse event reporting

We will follow the guidelines that require investigators to promptly notify the IRB (within days of the occurrence) when SAEs occur. SAEs will be defined as death, life threatening illness, hospitalization or prolongation of hospitalization, and persistent/significant disability. The IRB requires that any SAE that is unexpected and related or possibly related to the research intervention must be reported. SAEs that are unrelated to the research intervention do not have to be reported to the IRB (however, we will report these to the monitoring entity and NIH). Risks that are described in the protocol and consent form do not have to be reported as SAEs unless

the expected SAE occurs more frequently or is more serious than expected. One exception to this rule is in the case of a death. All deaths must be reported, whether or not the death was related to the research.

7.5 Data Security and Privacy

Beginning with the development process and throughout the research project, we will follow the privacy and security principles set forth at healthhit.gov. Our team is familiar with the importance of the privacy and security of personal health information to engender individual trust in the use of health IT applications. We have expertise and experience in this domain as we have developed a number of health IT systems funded through NIH and the Agency for Healthcare Research and Quality for persons living with HIV whose personal health information is usually held to higher security standards than traditional patients, as HIV has historically been a stigmatized disease.
We built the MyPEEPS App (NIMHD U01 MD011279) which is housed on the CUIMC IT servers. The CUIMC servers are located in a secure datacenter, with necessary redundancies. Currently the network can be accessed remotely via Virtual Private Network with a Citrix solution being developed. All servers have HIPAA compliant security.

CUIMC has an Information Security Office (ISO) that facilitates all aspects of information security risk management at CUIMC, with a particular focus on threat management and HIPAA compliance. This includes administration and enforcement of information security policies on campus. ISO also provides guidance to CUIMC schools and departments regarding any information security concerns they may have. The ISO collaborates with the entire CUIMC community to protect the confidentiality, integrity, and availability of critical information and computer resources. The ISO strives to implement secure computing infrastructure and practices with sensitivity to CUIMC's educational and research environment. Columbia University has an information security charter which is the foundation of all of the work carried out by Dr. Schnall and her research team. In specific, Dr. Schnall will work with the CUIMC IT server group and the information security office to protect the confidentiality, integrity, and availability of participants' data. Confidentiality means that information is only accessible to authorized users. Integrity means safeguarding the accuracy and completeness of data and processing methods. Availability means ensuring that authorized users, such as research participants, have access to data and associated information resources when required.

Prior to assent and consent, study participants will be informed as to what data the applications will collect. Data will be encrypted and stored securely on the CUIMC IT servers. As a starting point for ensuring privacy and security, all smartphones will be password–protected. In addition, there will be an additional password for the App so that only study subjects will be able to open the App.

7.5.1 Procedures to Ensure Compliance with Monitoring Plan and ReportingRequirements

Biweekly reports for the sites will be created by the study statistician to review relevant app engagement data, barriers with recruitment/enrollment and retention, laboratory and medical records, compliance with the protocol, and accuracy and completeness of the records. The

investigative team will schedule biweekly conference calls, and these reports will be briefly reviewed by the team. These regular reviews will ensure close communication between the research assistants, quickly identify missing data points, and ensure consistent management of any issues with the protocol between sites.

7.6 Data Analysis Plan for Aim 2

Assessment of feasibility and acceptability of the intervention (Table 5). We have specified the following measures of feasibility and acceptability: Retention Rates, Compliance Rates, Dose, Eligibility Criteria, Recruitment and Enrollment, Missing Data, Study Measures(68-70).

Table 5. Measures of Feasibility and Acceptability of MyPEEPS Mobile for YTM

Constructs	Measures	Threshold (if applicable)
Retention Rates	-How many enrollees remain in the study? -Are they about the same in both arms?	At least 80% will remain in the study.
Compliance Rates	What is the completion rate of app sessions by participants?	At least 80% will have completed at least 75% of the intervention content.
Dose	Is the dose of the intervention e.g., number of sessions adequate (assessment of paradata).	Does the dose need to be adjusted?
Eligibility Criteria	Are eligibility criteria acceptable, or do they need modification because they are too stringent?	Eligibility rates (number of individuals eligible among those approached)
Recruitment and Enrollment	What is the pace of recruitment? Barriers to recruitment and enrollment	• Rates of refusal (numberof refusals vs. enrolled among those approached) • Rates of no shows
Missing Data Measures	What is the extent and patterns of missing data? Length of time and burden to the respondents	The survey questions (Number and Type) may need to be adjusted

Study Outcomes. The pilot study will be used to assess the preliminary efficacy of MyPEEPS Mobile for YTM. Our primary outcome will be the number of condomless receptive anal and/or vaginal sex acts with either a cisgender male or transgender woman. To estimate the effect size for a larger clinical trial, we will focus on the primary outcome of: Condomless receptive anal or vaginal sex acts. The measures listed in Table 6 have been used in our MyPEEPS trialand piloted with 49 YTM as part of our formative work for this application. We will collect all measures at baseline, 3 and 6 months, other than demographic variables which will only be collected at baseline. We also ask participants to report on their own knowledge of their most recent partners' use of PrEP or ART medications. Given the unreliability of perceptions of partner-related risk in particular(71), we will use these data for a secondary sensitivity analysis (see below). This study is not powered for efficacy or tests of moderation or mediation; nonetheless, the purpose of the inclusion of these factors is to measure the impact of the intervention on

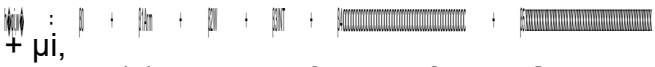
them as intermediate targets given their potential role in behavior change.

Table 6. Outcome Measures
Demographics
Sociodemographic (e.g., age, race/ethnicity level of education, housing status)
Newest Vital Sign(72)
Short Test of Functional Health Literacy (S-TOFHLA)(73)
Transgender Congruence Scale(74)
Measures of Hormone Use
Primary Outcome Measures
Condomless receptive anal and/or vaginal sex (adapted from AIDS-Risk Behavior Assessment)(68-70)
Intermediate Outcome Measures
Self-efficacy for safer sex and situational temptation for unsafe sex(75)
Condom Errors(76)
Health Protective Communication Scale(77)
HIV-Knowledge Questionnaire – HIV-KQ-18(78)
Alcohol and Substance Use(79)
Sexual Behavior Index**(80)**
Secondary Outcomes
nPEP and PrEP Use
Self-reported HIV and STI Testing
Partner(s) PrEP Use, PrEP Adherence or Viral Suppression (if partner is HIV+)
Program Evaluation
Knowledge of and beliefs about the content of the MyPEEPS Mobile intervention
MyPEEPS intervention acceptability and tolerability(81)
Paradata

Data Analysis. All multivariate analyses will be preceded by standard descriptive bivariate analyses to describe key variables and relationships among key variables. These analyses will include means, frequency tables, histograms, and examination of distributions. All statistical tests will be two-sided tests with the level of significance at 0.05(60).

Outcomes: This study will examine whether the intervention will reduce the number of condomless receptive anal or vaginal penile sex with either a cisgender male or transgender woman; the primary outcome is a count measure (Table 6 - Outcome Measures). We assume that all count outcome variables follow Poisson or negative binomial (NB) distribution, y~Poi(λ) or y~NB(λ, κ) and all percentage outcomes follow binomial distribution, y~bin(n, p). Let the expected value of outcome, E(y) = φ, so φ = λ for count oua tcomes and φ = p for binary outcomes. We propose the following generalized linear mixed model (GLMM) to analyze all outcomes. The level of analysis

will be assessed at each data point. For person i and data assess wave W (i.e., baseline, 3, and 6 months):



+ μi,

where h(.) Is the link function for the GLMM. We will use log-links (Poisson or NB regression) for count

Table 7. Codes for design variable s

	Intervention Arm			Delayed Intervention Arm		
Months	Arm	W	INT	Arm	W	INT
Baseline	0	0	0	1	0	0
3 mos	0	1	1	1	1	0
6 mos	0	2	1	1	2	1

outcomes and logit-links (logistic regression) for binary outcomes. μi iid~N(0, σj) are personal level random effects for the interceptor. Variables Arm, W, and INT are design variables. The codes for the design variables are presented in Table 7. Variable Arm is the indicator for intervention arms (0=intervention arm and 1=delayed intervention arm); variable W is data assess wave indicator (0=baseline, 1=3 months, 2=6 months); and variable INT is the intervention indicator (0=pre-intervention, and 1=post-intervention). COV is a vector of personal level covariates at the baseline, such as age, sex, etc., and XXXXXXXXXXXXXXXX is a vector of time-dependent covariates assessed at each wave of data for each subject controlling for potential bias between two arms. This model will include both baseline personal level covariates as well as personal-wave level covariates to control for different types of potential confounders. Regression parameter β3 is the mean value change for the outcome variables between pre- and post-intervention and measures the impact of the intervention on each outcome variable. For the Poisson or NB models, exp (β3) is the ratio of mean counts (i.e., risk ratio) between post and pre-intervention. For the logistic models, exp (β3) is the odds ratio between pre- and post-intervention. If the count outcome has excess 0s (for example, much greater than expected number of people who had 0 receptive condomless anal or vaginal sex act as comparison to number of people who had 1,2,..,etc. number of receptive condomless anal or vaginal sex acts), the above Poisson or negative binomial GLMMs can be extended to zero-inflated Poisson or negative binomial models(82).

Sensitivity Analysis: To address whether PrEP use by the partner or the viral suppression status of a HIV+ partner affects the outcome, we will ask participants if their partner(s) use PrEP, use PrEP regularly or if their partner is HIV+ are virally suppressed and we will conduct a counterfactual sensitivity analysis(83, 84), which includes the following steps: 1) We will examine if there is any difference in partners' PrEP use and/or HIV status between pre- and post- intervention. This comparison can be done using the same GLMM for the primary outcome, treating partners' PrEP use and/or HIV status as the outcome. 2) We will examine the impact (or association) of partners' PrEP use and/or HIV status on condomless anal sex based on a GLMM or LMM. 3) If there are difference in step 1) AND significant effects in step 2), our estimation of the impact of intervention on main outcome will be biased. We will correct estimates by estimating the true causal effect of impact on mainoutcome.

Secondary Outcomes: We will use GLMM to analyze secondary outcomes with appropriate choice of link functions according to the outcomes. All analyses will be done on the final data set (baseline n=80). As an objective of this R34, we will quantify intervention effect sizes of program impact on risky sexual behavior and substance use. To gauge effect sizes, we will use Cohen's d (85) and Hedge's g corrected for sample size(86), both of which express the average amount of individual change between experimental and control groups in terms of units of standard deviation. In addition, we will also estimate the correlations within outcomes across timepoints as the magnitude of this correlation can have significant impact on power to detect effects in repeated measures analyses. These estimates of effect size will enable us to accurately determine the sample size necessary to achieve adequate statistical power in future investigations of program efficacy within this population. We will use the following outcomes to estimate the statistical power for a larger study: (1) number of receptive condomless anal or vaginal sex acts with male partners (e.g., cisgender males and transgender women) during the past 3 months, and (2) number of HIV tests during the past 3 months. We will estimate the statistical power to examine overall effect with the total subjects to conduct stratified analysis to examine the effects in some subgroups (such as by sex and/or for some racial/ethnicity

subgroups). All power estimations will be based on α=0.05 and 2-sided tests. We will base our power estimates on the retention rate at the 3-month and 6-month follow up assessment for each study arm, the intra-cluster correlation.

Given these parameters, if the findings from the pilot study indicate that at post-intervention the number of receptive condomless anal or vaginal sex acts during the past 3 months decreased by 45% or a relative risk (RR) of 0.55, then for a future R01 study, we will have at least 99% power to detect such difference for a total sample size of 320. Secondly, for the stratified analyses, we will have 87% power to detect a relative risk of 0.55 in subgroups with a sample size of 64. For the HIV testing outcome, if the number of HIV tests during the past 3 months increases by 75% (i.e., RR
=1.75), a sample size of 320 participants will have an 84% power to detect such difference.
Paradata: we will assess participants' use of the App over time through the collection of paradata(87), specifically the page accessed, time stamp and device type. Paradata is considered "free" in that it does not require any additional effort from the user(88) **Data Analysis:** At the individual level, we will understand participants' use of the App over time through the collection of paradata(87) which is "free" in that it does not require any additional effort from the user(88). To explore barriers and facilitators to widespread implementation of MyPEEPS Mobile for YTM, we will collect data during intervention, implementation, and after the trial has ended. The primary paradata to be collected are page accessed, time stamp, and device type. From these data, we will derive the following use of data for each session: duration on each page, page progression through the application, time from login to result, and total time from login to logout. We will analyze the data at the individual-level (i.e., user-level), application-level, page-level, and session- level and assess how these differ by demographic characteristics, technology use, and outcome measures. Additionally, we will measure the amount in bytes of user data transmitted. Importantly, longitudinal analysis will determine if the user experience changes with repeated use. The paradata collected from each page will be analyzed to generate a "heatmap" of user-interaction (i.e., the distribution of activity for each link/button) that will inform user duration on each page of the App and user interaction with App content, contact pages, and the help page. We will explore usability issues with consideration for how many times users accessed help and what page of the App referred them to the help, implying the need for clarification. We will analyze differences in

aggregated data by demographic group (e.g., age) to better understand engagement with the intervention and potential facilitators and barriers to App use.

7.6.1 Data Analysis for Aim 3

All in-depth interviews will be transcribed verbatim and then coded. The development and application of a coding scheme is an integral component of the data analysis process. It enables the systematic examination and interpretation of the data related to the primary analytic foci. The coding scheme is conceptualized as a multilevel structure. At the highest level are the primary analytic foci coded as headings. Specific aspects or dimensions of the headings are assigned core codes. Specific aspects or dimensions of the core codes are assigned sub-codes. We will use NVivo™ (QSR International, Victoria, Australia), a software program for qualitative analysis, to facilitate the analysis.
The following 7 steps will be used to develop the coding scheme: Step 1: Identify the principal issues discussed by participants; Step 2: Construct definitions of the primary analytic themes;

Step 3: Develop and apply core codes and sub-codes to the initial set of interviews; Step 4: Develop a provisional coding scheme; Step 5: Test and refine the provisional coding scheme; Step 6: Reconcile coding differences and construct an updated and final coding scheme; Step 7: Apply the coding scheme to the full data set and assess inter-coder reliability. After all transcripts have been coded, we will extract and examine the content of text segments linked to core codes and sub- codes relevant to understanding barriers and facilitators to the use of the MyPEEPS App. Based on the coded data, we will propose ways in which certain themes are analytically related. A careful examination of the coded text will reveal the associations among these themes and may lead to more refined data searches. Once we establish patterns of relationships among themes and issues, we will identify participants' accounts that support or refute these patterns. Identifying and accounting for cases that deviate from an interpretative pattern enables us to test and confirm the pattern's validity and robustness.

Triangulation of Findings. We will examine changes in HIV risk behaviors and its relationship to factors including but not limited to changes in substance use, alcohol use, stigma, victimization. We will triangulate the findings from our quantitative outcome measures (Aim 2) with the findings from our qualitative data (Aim 3) to better understand participants' decisions for their HIV risk behaviors.

7.7 Missing Data

Missing data may occur in the proposed study in several ways. First, it may be due to item non-response. In these cases, we will prorate total scores for a measure by taking an average score on the measure and multiplying it by the total number of items in the scale. Attrition can result in missing data due to missed assessments or dropout from the study. Prior to performing any outcome analyses, we will evaluate the amount, reasons, and patterns of missing data. Missing data unrelated to the outcome of interest will be considered missing completely at random (MCAR), and complete case analysis will still generate unbiased estimates.(89) For the missing values at the baseline or partial baseline collected data, we will use a multiple imputation approach.(89) We will conduct sensitivity analyses to compare estimates of treatment effects with and without multiple imputation to assess the effect of missing data on statistical inference.

8.1 HUMAN SUBJECTS PROTECTIONS

8.2 Informed Consent and Assent

The study plan, advertisements, or recruitment letters, lay description of the study, and all consent forms will be submitted to the IRB following proposal acceptance and prior to study initiation. MPI, Dr. Schnall, will be responsible for obtaining IRB approval for this study. Recruitment for study participation will occur following IRB approval. The MPIs will delegate study task to research staff including determining eligibility for inclusion, explaining the purpose of the study, answering any questions, and obtaining e-assent/consent from the participants. Individuals who agree to participate will sign an e-assent/consent form. Potential risks and strategies for risk management will be carefully explained as part of informed e-assent/consent procedures. All HIPAA requirements will be applied to this study.

8.2.1 Consent and Assent Process

Written informed e-assent will obtained from study participants under age 18. Participants at age 17 will be considered children for purposes of study activities. As such, they will complete informed assent for these portions of the study. Study participants ages 18 and above will provide written informed consent. If a respondent asks any questions about the study, an on-site research assistant will clarify or answer questions. The participant's ability to not respond to any study questions and/or terminate participation at any time will be stated clearly in consent forms.

8.2.2 Parental consent

Consistent with our prior studies in this population, we will not require parental consent for study enrollment. Parental consent may decrease participation rates because some youth (17-year-olds) will fear that they may be "outed" as a result of participation. Disclosure of sexual orientation or gender identity may place participating youth at risk for parental harassment, abuse, or expulsion from the home. The nature and scope of the proposed research do not pose more than "minimal risk" to participants, or that "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" (45 CFR Part 46.102). Study measures are standard in this population, as are waivers of parental permission for survey and interview studies.

8.2 Waiver of Parental Written Consent and Screening Procedure Written Consent

Each study site has experience conducting HIV prevention research with minors. We will be applying for a waiver of written informed consent from the parents of study participants because the involvement of children in this research meets the criteria for waiving parent permission (45 CFR 46.116(d)). The study qualifies for a waiver of parental consent as the following criteria are met in this study:

- The research involves no more than minimal risk to the subjects - The study does not place the patient at any additional risk than using their smartphones during their everyday lives.

  The only other risk to participants is a breach of their protected health information, and we have put systems in place to protect their identity.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects - If parents are required to consent their children then this may present a breach of confidentiality related to participants' sexuality and sexual behaviors.
- The research could not practicably be carried out without the waiver or alteration - If consent is required from parents then this may jeopardize the confidentiality of our study participants' health behaviors and may place study participants at increased risk of adverse outcomes associated with disclosure of their sexual orientation to their parents. Past research has shown a higher risk of familial childhood maltreatment among lesbian, gay, and bisexual individuals than among heterosexual individuals.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation - All study subjects will be given a copy of the written assent form which will include contact information of our study team as well as referral information.

To compensate for the waiver of parental consent, participants receive the described formal individual assessment of capacity to consent (above) to ensure their understanding of study

goals, procedures, and risks from disclosure of sensitive information. Consistent with national policy recommendations from the Society for Adolescent Medicine, requiring parental permission for the proposed study would have a number of possible negative effects, including: (1) reducing the validity of the findings by effectively eliminating potential participants unwilling to share permission forms with their parents/guardians; (2) increasing risk to some youth whose parents have a negative response to the material in the permission forms that would (correctly) suggest their child has a minority or alternative sexual orientation; and (3) contributing little to actual subject protection, given the minimal risk of study participation.

We are also requesting a waiver of documentation of consent for online screening procedures. The screening information will only be kept electronically in REDCap, which is a secure, CUMC approved system.

8.3 Vulnerable Subjects: Protecting Against/Minimizing Potential Risk

8.3.1 Procedures in the event of a reactive HIV test.

In the event a participant has a reactive HIV test, study team members will counsel the participant regarding the meaning of their result. Specifically, the study team will reiterate with the participant that:

- Their result is a preliminary positive, and it is likely that they are infected with HIV,
- The preliminary positive result needs to be verified with confirmatory testing,
- They need to return for the results of their confirmatory testing,and
- Resources for counseling and referral to care are available to them.

The participant will be referred for follow-up testing and care. We have one physician and one nurse as part of our investigator team.

8.4 Risks

8.4.1 Overview of Potential Risks

There is no more than a minimal risk associated with any of the proposed study activities. The study activities meet the general definition found in Subpart A (46.102) that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological assessments or tests. The risks of participating in this study are few. Potential risks are those related to venipuncture, discomfort with study interview questions, and potential breaches of confidentiality. It is possible that certain questions on the survey may make participants feel uncomfortable, but participants are free to decline to answer any questions. Additionally, clinical study sites have co-located mental health and/or counseling services that may be consulted should a participant enter crisis. Participation in research can involve loss of privacy. All study data will be maintained on Columbia University Irving Medical Center (CUIMC) and Lurie Children's Hospital servers that are secure and HIPAA compliant. All signed consent forms, study data, and payment receipts used in this study will be kept in locked files at both sites which only the investigators can access. We will also receive a Federal Certificate of Confidentiality which will protect against attempts by law enforcement or other government

agencies to access our data.

8.4.2 General Risks

There may be risks or discomforts in participating in this study. Participants may feel uncomfortable with the HIV prevention information that is provided and completing some questions in the survey. Participants may skip any HIV information or questions that may make them feel uncomfortable or stop the research procedure. People around may observe participants using the MyPEEPS Mobile application. If participants are concerned about people seeing them use of MyPEEPS Mobile, it is important that they access the application in private location.

8.4.3 Loss of confidentiality

A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of confidentiality or privacy means having personal information shared with someone who is not on the study team and was not supposed to see or know about your information. All study data will be stored in password protected computers or file cabinets in locked offices. All research team members will pass the protection of human subjects and research HIPAA exams and sign a protocol-specific conflict of interest. All procedures have been designed to protect each participant's privacy and allow for anonymous participation. All study data will be maintained in a completely secure and HIPAA compliant environment. All CUIMC servers have HIPAA compliant security

8.5 Social Impact Events

Individuals enrolled in this study may experience personal problems resulting from the study participation. Such problems are termed social impact events. Although study sites will make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that participants may experience stigmatization or discrimination as a result of being perceived as being HIV infected or at risk for HIV infection. For example, participants could be treated unfairly, or could have problems being accepted by their families and/or communities. Problems may also occur in circumstances in which study participation is not disclosed, such as impact on employment related to time taken for study visits.

In the event that a participant reports a social impact event, every effort will be made by study staff to provide appropriate assistance, and/or referrals to appropriate resources. Social impact events are documented and reviewed on a scheduled basis by the protocol team leadership with the goal of reducing their incidence and enhancing the ability of study staff to mitigate them when possible.

Social impact events that are judged by the MPIs/designee to be serious, unexpected, or more severe or frequent than anticipated, will be reported to the responsible site's Ethics Committee/Institutional Review Board (EC/IRB) promptly, or otherwise in accordance with the EC/IRB's requirements.

8.6 Benefits

The potential benefits to an individual participant in the study are not known. The potential benefits of the study to others could be considerable. If our hypotheses are true, this study will

make a significant contribution towards improving HIV incidence in YTM. This study has not been designed for the direct benefit of its participants; however, there are a number of ways in which they may derive benefit, such as awareness of HIV status, increased access to HIV prevention tools (e.g., testing, PrEP) and HIV services, if a participant sero-converts. The proposed research will inform the delivery of HIV prevention messages. The knowledge gained will contribute to the body of knowledge regarding the use of health information technology for improving the lives of YTM at risk for HIV. The avoidance of HIV throughout study participation will be a significant personal benefit to participants.

8.7 Participant Privacy and Confidentiality

Access to individually identifiable private information about human subjects. Access to individually identified private information about human subjects will be limited to research team members who collect and manage the data, the Project Director, and the MPIs. De-identified data will be accessible to all members of the research team involved in the data analysis.

Our study team is extremely prudent in keeping subject data secure and confidential. All laboratory specimens, evaluation forms, reports, and other records will be identified by a unique coded number to maintain participant confidentiality. The material, records, and data obtained through participation in the study will be specifically for research purposes. Existing health records may be used with the permission of the participants. Materials will be obtained by trained clinical staff at each study site. Data will be stored using Research Electronic Data Capture (REDCap) at each respective performance site, and then the completely deidentified data will be merged at CUIMC. All laboratory specimens will be identified *only* by the identification number. The code linking the participant identification number to subject identifying information (name, address, etc.) is maintained at the clinical sites through REDCap, and only authorized site personnel have access to the code. Limited individually identifiable private information is collected that is essential for processing participant payments and for analysis purposes.

All study data will be stored in password-protected computers or file cabinets in locked offices. All research team members will pass the protection of human subjects and HIPAA research exams and sign a protocol-specific conflict of interest. Risks will be minimized by not including personal

identifying information on the forms, when possible, and by conducting interviews and collection of personal information in a private setting. All data will be collected using unique patient identification codes. All laboratory specimens, evaluation forms, reports, and other records will be identified by a coded number to maintain participant confidentiality. All records will be stored in a locked file cabinet. Study data from both sites will be collected and managed using REDCap. REDCap is a secure web application designed to support data capture for research studies, providing user- friendly web-based case report forms, real-time data entry validation (e.g., for data types and range checks), audit trails, and a de-identified data export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). REDCap data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team. This iterative development and testing process results in a well-planned data collection strategy for individual studies. REDCap also includes a powerful tool for building and managing online surveys. The research team can create and design surveys in a web browser and engage potential respondents using a variety of notification methods. REDCap is flexible enough to be used for a variety of types of research and provides an intuitive user

interface for database and survey design and data entry. Lastly, clinical information will not be released without written permission of the participant, except as necessary for monitoring by the IRB or the NIH.

8.7.1 Confidentiality of Study Data

We have developed systematic protocols for data handling and storage over multiple cohort studies. To protect the integrity of the participant's data, the RA will assign each participant a unique PID at study enrollment. This code number will be used for all study data. We will maintain a list of participants with links between identifying information and code numbers for the sole purpose of avoiding any duplication in completion of the survey. Only the PIs, RAs, and Project Director will have access to these lists, which will be kept behind double-locks or on a secure server with password protected access. Computer files consist of the tracking database (REDCap), and study data files downloaded from the database. Tracking files are maintained in a highly secure scheduling and monitoring database which both sites can access. This database contains all contact information and is used to schedule and track study visits; it is completely password protected and user access and privileges will be managed by the data manager and Project Director. The tracking database stores contact preferences including information the participant agreed to provide for the purposes of tracking and communication; all communications strictly follow the participants' contact limitations. Data files are exported from REDCap and imported into the SPSS database for storage and analysis. Computer data files never have any identifying information and are encrypted for transfer between study sites. Data files do not include information that could be used to identify the participant from the data file alone. Columbia University will provide a standards-compliant (HIPAA, HHS Cybersecure) private cloud server for the hosting of application content and user data for the duration of the application deployment. This is a secure system and will be further protected by login credentials for limited access to protect participant confidentiality. Participants will also be encouraged to choose a private location to program a password for the application and complete the intervention modules for additional security. They will be prompted to log-out of the website after completing or progressing through any given module.

8.8 Certificate of Confidentiality

This research specifically targets a vulnerable population, children - YTM age 17. We will take every available step to minimize the risk of identifying/linking data being subpoenaed, stolen, or inadvertently released. First, per Section 2012 of the 21st Century Cures Act as implemented in the 2017 NIH Certificates of Confidentiality Policy, all ongoing or new research funded by NIH as of December 13, 2016 that is collecting or using identifiable, sensitive information is automatically issued a CoC. 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 participant (i.e., about

whom the investigator maintains identifying information) during any time the Certificate is in effect." 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 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.

8.9 Unexpected and Serious Adverse Event Reporting

A detailed monitoring plan will be included as part of the study protocol, submitted to the IRB, and reviewed and approved by the NIMH before the study begins. Prior to initiation of the study, agreement about the data safety monitoring plan will be confirmed to ensure the safety of subjects and the validity and integrity of the data. The research coordinator at each site will report serious adverse events (SAEs) that are unexpected and study-related immediately to a study physician who will convey this information to the study team, IRB, and the NIH. All AEs and SAEs will be captured, reports will be completed, and information will be entered into the study database. A safety report will detail all serious and unexpected AEs or other unanticipated problems that involve risk to study participants or others and whether these appeared to be related to the study- based interventions or research assessment protocols. All AEs will be reviewed every 6 months, or sooner, with the designated safety Data Safety and Monitoring Board.

8.10 ClinicalTrials.gov

This trial and protocol will be registered in ClinicalTrials.gov.

9.0 PUBLICATION POLICY

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

10.0 REFERENCES

1. Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. Estimating the Prevalence of HIVand Sexual Behaviors Among the US Transgender Population: A Systematic Review and Meta-Analysis, 2006– 2017. American journal of public health. 2018;109(1):e1-e8. doi: 10.2105/AJPH.2018.304727.
2. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhea and chlamydia reinfection is associated with increased risk of HIV seroconversion. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2010;53(4):537-43.
3. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sexually transmitted infections. 1999;75(1):3-17.
4. Beck EC, Birkett M, Armbruster B, Mustanski B. A data-driven simulation of HIV spread among young men who have sex with men: the role of age and race mixing, and STIs. Journal of acquired immune deficiency syndromes (1999). 2015;70(2):186.
5. Bockting WO, Miner MH, Swinburne Romine RE, Hamilton A, Coleman E.Stigma, mental

health, and resilience in an online sample of the US transgender population. American journal of public health. 2013;103(5):943-51.
6. Reisner SL, Gamarel KE, Dunham E, Hopwood R, Hwahng S. Female-to-male transmasculine adult health: a mixed-methods community-based needs assessment. Journal of the American Psychiatric Nurses Association. 2013;19(5):293-303.
7. Reisner SL, Pardo ST, Gamarel KE, White Hughto JM, Pardee DJ, Keo-Meier CL. Substance use to cope with stigma in healthcare among U.S. female-to-male trans masculine adults. LGBT Health. 2015;2(4):324-32. doi: 10.1089/lgbt.2015.0001.
8. Golub SA, Fikslin RA, Starbuck L, Klein A. High Rates of PrEP Eligibility but Low Rates of PrEP Access Among a National Sample of Transmasculine Individuals. J Acquir Immune Defic Syndr. 2019;82(1):e1-e7. Epub 2019/06/25. doi: 10.1097/QAI.0000000000002116. PubMed PMID: 31232834; PMCID: PMC6692190.
9. Reisner SL, Moore CS, Asquith A, Pardee DJ, Sarvet A, Mayer G, Mayer KH. High risk andlow uptake of pre-exposure prophylaxis to prevent HIV acquisition in a national online sample of transgender men who have sex with men in the United States. J Int AIDS Soc. 2019;22(9):e25391. Epub 2019/09/20. doi: 10.1002/jia2.25391. PubMed PMID: 31536171; PMCID: PMC6752156.
10. Herbst JH, Beeker C, Mathew A, McNally T, Passin WF, Kay LS, Crepaz N, Lyles CM, Briss P, Chattopadhyay S, Johnson RL. The Effectiveness of Individual-, Group-, and Community-Level HIV Behavioral Risk-Reduction Interventions for Adult Men Who Have Sex with Men: A Systematic Review. American Journal of Preventive Medicine. 2007;32(4, Supplement):38-67. doi: http://dx.doi.org/10.1016/j.amepre.2006.12.006.
11. Schnall R, Cimino JJ, Bakken S. Development of a prototype continuity of care record with context-specific links to meet the information needs of case managers for persons living with HIV. International journal of medical informatics. 2012. Epub 2012/05/29. doi: 10.1016/j.ijmedinf.2012.05.002. PubMed PMID: 22632821.
12. Bennett GG, Glasgow RE. The delivery of public health interventions via the Internet: actualizing their potential. Annual review of public health. 2009;30:273-92. doi: 10.1146/annurev.publhealth.031308.100235. PubMed PMID: 19296777.
13. Schnall R, Wantland D, Velez O, Cato K, Jia H. Feasibility testing of a web-based symptom self- management system for persons living with HIV. J Assoc Nurses AIDS Care. 2014;25(4):364-71. doi: 10.1016/j.jana.2013.09.002. PubMed PMID: 24434198; PMCID: 4057945.
14. Moskowitz D, Melton, D., & Owczarzak, J. , 77(1), 20-26. . PowerON: the use of instant message counseling and the Internet to facilitate HIV/STD education and prevention. Patient Educ Couns. 2009;77(1):20-6. doi: 10.1016/j.pec.2009.01.002.
15. Wei C, Lim S, Guadamuz T, Koe S. Virtual Versus Physical Spaces: Which Facilitates Greater HIV Risk Taking Among Men Who Have Sex with Men in East and South-East Asia? AIDS and Behavior. 2013:1-8. doi: 10.1007/s10461-013-0628-4.
16. Williams M, Bowen A, Ei S. An evaluation of the experiences of rural MSM who accessed an online HIV/AIDS health promotion intervention. Health promotion practice. 2010;11(4):474-82. doi: 10.1177/1524839908324783. PubMed PMID: 19116419; PMCID: 2916959.
17. Hightow-Weidman L, Pike, E., Fowler, B., Matthews, D., Kibe, J., McCoy, R., & Adimora, A. . HealthMpowerment.org: Feasibility and acceptability of delivering an Internet intervention to young Black men who have sex with men. AIDS Care. 2012;24(7):910-20. doi: 10.1080/09540121.2011.647677.
18. Williams ML, Bowen AM, Horvath KJ. The social/sexual environment of gay men residing in a rural frontier state: implications for the development of HIV prevention programs. The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association. 2005;21(1):48-55. PubMed PMID: 15667009; PMCID: 2614671.
19. Paul ME, Castillo M, Emmanuel P, Bauermeister JA, Mena LA, Sullivan PS, Hightow-Weidman LB. Scale up mHealth HIV interventions: site and public health perspectives and lessons learned from P3. Mhealth. 2021;7:38. Epub 2021/04/27. doi: 10.21037/mhealth-20-65. PubMed PMID:33898607;

PMCID: PMC8063006.
20. Donenberg GR, Pao M. Youths and HIV/AIDS: Psychiatry's Role in a Changing Epidemic. Journal of the American Academy of Child & Adolescent Psychiatry. 2005;44(8):728-47. doi: http://dx.doi.org/10.1097/01.chi.0000166381.68392.02.
21. Balaji A, Bowles K, Le B, et al. High HIV incidence and prevalence and associated risk factors among young MSM, 2008. AIDS. 2013;27:269-78.
22. Hidalgo M, Kuhns L, Hotton A, Johnson A, Mustanski B, Garofalo R. The MyPEEPS Randomized Controlled Trial: A Pilot of Preliminary Efficacy, Feasibility, and Acceptability of a Group-Level, HIV Risk Reduction Intervention for Young Men Who Have Sex with Men. Arch Sex Behav. 2015;44(2):475-85. doi: 10.1007/s10508-014-0347-6.
23. Gordian-Arroyo A, Garofalo R, Kuhns LM, Pearson C, Bruce J, Batey DS, Radix A, Belkind U, Hidalgo MA, Hirshfield S, Schrimshaw EW, Schnall R. Awareness, Willingness, and Perceived Efficacy of Pre-exposure Prophylaxis among Adolescent Sexual Minority Males. J Urban Health. 2020. Epub 2020/08/14. doi: 10.1007/s11524-020-00447-5. PubMed PMID: 32789625.
24. Ignacio M, Garofalo R, Pearson C, Kuhns LM, Bruce J, Scott Batey D, Radix A, Belkind U, Hidalgo MA, Hirshfield S, Schnall R. Pilot feasibility trial of the MyPEEPS mobile app to reduce sexual risk among young men in 4 cities. JAMIA Open. 2019;2(2):272-9. Epub 2019/07/12. doi: 10.1093/jamiaopen/ooz008. PubMed PMID: 31294422; PMCID: PMC6603441.
25. Kuhns LM, Garofalo R, Hidalgo M, Hirshfield S, Pearson C, Bruce J, Batey DS, Radix A, BelkindU, Jia H, Schnall R. A randomized controlled efficacy trial of an mHealth HIV prevention intervention for sexual minority young men: MyPEEPS mobile study protocol. BMC Public Health. 2020;20(1):65. Epub 2020/01/17. doi: 10.1186/s12889-020-8180-4. PubMed PMID: 31941475; PMCID: PMC6964028.
26. Schnall R, Kuhns L, Pearson C, Bruce J, Batey DS, Radix A, Belkind U, Hidalgo MA, Hirshfield S, Ganzhorn S, Garofalo R. Preliminary Results from a Pragmatic Clinical Trial of MyPEEPS Mobile to Improve HIV Prevention Behaviors in Young Men. Stud Health Technol Inform. 2020;270:1365-6. Epub 2020/06/24. doi: 10.3233/SHTI200444. PubMed PMID: 32570661.
27. Schnall R, Kuhns LM, Hidalgo MA, Powell D, Thai J, Hirshfield S, Pearson C, Ignacio M, Bruce J, Batey DS. Adaptation of a group-based HIV risk reduction intervention to a mobile app for young sexual minority men. AIDS Education and Prevention. 2018;30(6):449-62.
28. James SE, Herman, J.L., Rankin, S., Keisling, M., Mottet, L., Anafi, M. The Report of the2015 U.S. Transgender Survey Washington, D.C.: National Center for Transgender Equality; 2015. Available from: https://transequality.org/sites/default/files/docs/usts/USTS-Full-Report-Dec17.pdf.
29. Gass BV, Horvath KJ, Marrow E, Rood BA, Pantalone DW. Associations Between Social Support Availability and HIV Risk and Protective Factors in a U.S. Sample of Adults with Diverse Transgender

Identities. LGBT Health. 2021;8(1):60-7. Epub 2020/12/29. doi: 10.1089/lgbt.2020.0035. PubMed PMID: 33370219.
30. Todd K, Peitzmeier SM, Kattari SK, Miller-Peruse M, Sharma A, Stephenson R. Demographic and Behavioral Profiles of Nonbinary and Binary Transgender Youth. Transgend Health. 2019;4(1):254-61. Epub 2019/10/24. doi: 10.1089/trgh.2018.0068. PubMed PMID: 31641692; PMCID:PMC6802728.
31. Centers for Disease Control and Prevention. Lifetime Risk of HIV Diagnosis 2016 [updated February 2323 April 2018]. Available from: https://www.cdc.gov/nchhstp/newsroom/2016/croi-press-release-risk.html.
32. Fauci AS, Redfield RR, Sigounas G, Weahkee MD, Giroir BP. Ending the HIV Epidemic: A Plan for the United States. JAMA. 2019;321(9):844-5. doi: 10.1001/jama.2019.1343.
33. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. Journal of biomedical informatics. 2009;42(2):377-81.
34. Ballard AM, Cardwell T, Young AM. Fraud detection protocol for web-based research among men who have sex with men: development and descriptive evaluation. JMIR Public Health Surveill. 2019;5(1):e12344.

35. Teitcher JE, Bockting WO, Bauermeister JA, Hoefer CJ, Miner MH, Klitzman RL. Detecting, preventing, and responding to "fraudsters" in internet research: ethics and tradeoffs. The Journal of Law, Medicine & Ethics. 2015;43(1):116-33.
36. Ignacio M, Garofalo R, Pearson C, Kuhns LM, Bruce J, D Batey S, Radix A, Belkind U, Hidalgo MA, Hirshfield S. Pilot feasibility trial of the MyPEEPS mobile app to reduce sexual risk among young men in 4 cities. JAMIA Open. 2019.
37. Schnall R, Kuhns L, Hidalgo M, Hirshfield S, Pearson C, Radix A, Belkind U, Bruce J, Batey DS, Garofalo R. Development of MyPEEPS Mobile: A Behavioral Health Intervention for Young Men. Studies in health technology and informatics. 2018;250:31-.
38. Schnall R, Kuhns L, Pearson C, Bruce J, Batey DS, Radix A, Belkind U, Garibay-Rodriguez R, Grimball R, Hidalgo M, editors. Comparison of Recruitment Strategies for Young Men's Participation in a HIV Prevention Trial. APHA's 2019 Annual Meeting and Expo (Nov 2-Nov 6); 2019: American Public Health Association.
39. Cho H, Powell D, Pichon A, Thai J, Bruce J, Kuhns LM, Garofalo R, Schnall R. A mobile health intervention for HIV prevention among racially and ethnically diverse young men: usability evaluation. JMIR mHealth and uHealth. 2018;6(9):e11450.
40. Cho H, Powell D, Pichon A, Kuhns LM, Garofalo R, Schnall R. Eye-tracking retrospective think-aloud as a novel approach for a usability evaluation. International journal of medical informatics. 2019;129:366-73.
41. Nielsen J, Molich R. Heuristic evaluation of user interfaces. Proceedings of the SIGCHI Conference on Human Factors in Computing Systems; Seattle, Washington, USA. 97281: ACM; 1990.p. 249-56.
42. Sheehan B, Lee Y-J, Rodriguez M, Tiase V, Schnall R. A Comparison of Usability Factors of Four Mobile Devices for Accessing Healthcare Information by Adolescents. Appl Clin Infor. 2012;3(4):356-66.
43. Lee Y, Johnson SB, Trembowelski S, Schnall R, Sheehan B, Bakken S. Cognitive walkthrough evaluation of an investigator profiles directory. . Proc AMIA Annu Fall Symp. 2011.
44. Schnall R, Kaufman D, Hyun S, Bakken S, editors. Cognitive Evaluation of Case Managers' Use of a Continuity of Care Document for Persons Living with HIV AMIA Annual Symposium; 2009; San Francisco, CA.
45. Bertini E, Gabrielli S, Kimani S, editors. Appropriating and assessing heuristics for mobile computing. Advanced Visual Interfaces International Working Conference; 2006; Venezia, Italy.
46. Gibson L, Gaffey E, Spendlove J, editors. The Usability Factor: More than just a Pretty Interface. 8th International Congress in Nursing Informatics; 2003; Rio de Janeiro, Brazil.
47. Nielson J. Ten Usability Heuristics 2005 [updated 2005]. Available from: http://www.useit.com/papers/heuristic/heuristic_list.html.
48. Bright T, Bakken S, Johnson S. Heuristic evaluation of eNote: an electronic notes system. New York2006.
49. Nielsen J. Heuristic evaluation. In: Nielsen J, Mack RL, editors. Usability Inspection Methods. New York, NY: John Wiley & Sons; 1994.
50. Faulkner L. Beyond the five-user assumption: benefits of increased sample sizes in usability testing. Behav Res Methods Instrum Comput. 2003;35(3):379-83. Epub 2003/11/01. PubMed PMID: 14587545.
51. Yen PY, Wantland D, Bakken S. Development of a Customizable Health IT Usability Evaluation Scale. AMIA Annual Symposium proceedings / AMIA Symposium AMIA Symposium. 2010;2010:917-21. PubMed PMID: 21347112; PMCID: 3041285.
52. Davis F. Perceived usefulness, perceived ease of use, and user acceptance of information technology. MIS Quarterly. 1989;13(3):319-40.
53. Brown W, 3rd, Yen PY, Rojas M, Schnall R. Assessment of the Health IT Usability Evaluation Model (Health-ITUEM) for evaluating mobile health (mHealth) technology. Journal of biomedical

informatics. 2013;46(6):1080-7. doi: 10.1016/j.jbi.2013.08.001. PubMed PMID: 23973872; PMCID: 3844064.
54. Lloyd CE, Johnson MR, Mughal S, Sturt JA, Collins GS, Roy T, Bibi R, Barnett AH. Securing recruitment and obtaining informed consent in minority ethnic groups in the UK. BMC Health Serv Res. 2008;8:68. Epub 2008/04/01. doi: 1472-6963-8-68 [pii] 10.1186/1472-6963-8-68 [doi]. PubMed PMID: 18373876; PMCID: 2311303.
55. Swanson GM, Ward AJ. Recruiting minorities into clinical trials: toward a participant-friendly system. J Natl Cancer Inst. 1995;87(23):1747-59. Epub 1995/12/06. PubMed PMID: 7473831.
56. Altman DG, Bland JM. Treatment allocation in controlled trials: why randomise? BMJ. 1999;318(7192):1209-.
57. Hedden SI, Woolsen RF, Malcolm RJ. Randomization in substance abuse clinical trials. Substance Abuse Treatment, Prevention, and Policy. 2006;1:6.
58. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. J Clin Epi 2010;. BMC Medicine 2010;8(18). Epub 24 march 2010.
59. Vickers AJ. How to randomize. Journal of the Society for Integrative Oncology. 2006;4(4):194-8. PubMed PMID: 17022927; PMCID: 2596474.
60. Lyles CM, Crepaz N, Herbst JH, Kay LS. Evidence–Based HIV Behavioral Prevention From the Perspective of the CDC's HIV/AIDS Prevention Research Synthesis Team. AIDS Education and Prevention. 2006;18(supp):21-31. doi: 10.1521/aeap.2006.18.supp.21.
61. Garofalo R, Kuhns LM, Hotton A, Johnson A, Muldoon A, Rice D. A Randomized Controlled Trial of Personalized Text Message Reminders to Promote Medication Adherence Among HIV-Positive Adolescents and Young Adults. AIDS Behav. 2016;20(5):1049-59. Epub 2015/09/13. doi: 10.1007/s10461- 015-1192-x. PubMed PMID: 26362167; PMCID: PMC4788595.
62. Green L, Kreuter, M., Deeds, S., Partridge, K. Health education planning: Adiagnostic approach. Mountain View, CA: Mayfield; 1980.
63. Kukafka R, Johnson SB, Linfante A, Allegrante JP. Grounding a new information technology implementation framework in behavioral science: a systematic analysis of the literature on IT use. Journal of biomedical informatics. 2003;36(3):218-27. Epub 2003/11/15. doi: 10.1016/j.jbi.2003.09.002. PubMed PMID: 14615230.
64. Odlum M, Gordon P, Camhi E, Schnall R, Teixeira P, Bakken S. Perceptions of predisposing, enabling, and reinforcing factors influencing the use of a continuity of caredocument in special needs PLWH. J Health Care Poor Underserved. 2012;23(4):1457-76. Epub 2012/01/01. doi: 10.1353/hpu.2012.0172. PubMed PMID: 23698661.
65. Schnall R, Gordon P, Camhi E, Bakken S. Perceptions of factors influencing use of an electronic record for case management of persons living with HIV. AIDS Care. 2011;23(3):357-65. Epub 2011/02/25. doi: 10.1080/09540121.2010.507745. PubMed PMID: 21347899; PMCID: PMC3129034.
66. Guba EG. Criteria for assessing the trustworthiness of naturalistic inquiries. Educational Communication and Technology Journal1981;29(2):75-91.
67. Garofalo R, Kuhns LM, Reisner SL, Biello K, Mimiaga MJ. Efficacy of an Empowerment-Based, Group-Delivered HIV Prevention Intervention for Young Transgender Women: The Project LifeSkills

Randomized Clinical Trial. JAMA Pediatr. 2018;172(10):916-23. doi: 10.1001/jamapediatrics.2018.1799. PubMed PMID: 30105381.
68. Donenberg GR, Emerson E, Bryant FB, Wilson H, Weber-Shifrin E. Understanding AIDS-Risk Behavior Among Adolescents in Psychiatric Care: Links to Psychopathology and Peer Relationships. Journal of the American Academy of Child and Adolescent Psychiatry. 2001;40(6):642-53. PubMed PMID: PMC1201503.
69. Garofalo R, Mustanski BS, McKirnan DJ, Herrick A, Donenberg GR. Methamphetamine and Young Men who have Sex with Men: Patterns, Correlates and Consequences of Use. Archives of pediatrics & adolescent medicine. 2007;161(6):591-6. doi: 10.1001/archpedi.161.6.591. PubMed PMID:

PMC3985401.
70. Garofalo R, Herrick A, Mustanski BS, Donenberg GR. Tip of the Iceberg: Young Men Who Have Sex With Men, the Internet, and HIV Risk. American journal of public health. 2007;97(6):1113-7. doi: 10.2105/AJPH.2005.075630. PubMed PMID: PMC1874202.
71. Gallagher T, Link L, Ramos M, Bottger E, Aberg J, Daskalakis D. Self-Perception of HIV Risk and Candidacy for Pre-Exposure Prophylaxis Among Men Who Have Sex with Men Testing for HIV at Commercial Sex Venues in New York City. LGBT Health. 2014;1(3):218-24. Epub 2014/09/01. doi: 10.1089/lgbt.2013.0046. PubMed PMID: 26789715.
72. Weiss BD, Mays MZ, Martz W, Castro KM, DeWalt DA, Pignone MP, Mockbee J, Hale FA. Quick Assessment of Literacy in Primary Care: The Newest Vital Sign. The Annals of Family Medicine. 2005;3(6):514-22. doi: 10.1370/afm.405.
73. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief test to measure functional health literacy. Patient Education and Counseling. 1999;38(1):33-42. doi: http://dx.doi.org/10.1016/S0738-3991(98)00116-5.
74. Kozee HB, Tylka TL, Bauerband LA. Measuring transgender individuals' comfort with gender identity and appearance: Development and validation of the Transgender Congruence Scale. Psychology of Women Quarterly. 2012;36(2):179-96.
75. Parsons JT, Halkitis PN, Bimbi D, Borkowski T. Perceptions of the benefits and costs associated with condom use and unprotected sex among late adolescent college students. Journal of Adolescence. 2000;23(4):377-91. doi: http://dx.doi.org/10.1006/jado.2000.0326.
76. CROSBY RA, SANDERS SA, YARBER WL, GRAHAM CA, DODGE B. Condom Use Errors and Problems Among College Men. Sexually Transmitted Diseases. 2002;29(9):552-7. PubMed PMID: 00007435-200209000-00010.
77. Catania JA. The health protective communication scale. Davis CM, Yarber WL, Bauserman R, Schreer G, Davis SL, editors. Thousand Oaks, CA: Sage Publications;1998.
78. Carey MP, Schroder KE. Development and psychometric evaluation of the brief HIV Knowledge Questionnaire. AIDS Educ Prev. 2002;14(2):172-82. Epub 2002/05/10. PubMed PMID: 12000234; PMCID: 2423729.
79. National Institutes of Drug Abuse. NIDA-Modified Assist 2015. Availablefrom: file:///C:/Users/rb897/Desktop/APA_DSM5_Level-2-Substance-Use-Child-Age-11-to-17.pdf.
80. Hennessy M, Bleakley A, Fishbein M, Jordan A. Validating an Index of Adolescent Sexual Behavior Using Psychosocial Theory and Social Trait Correlates. AIDS and behavior. 2008;12(2):321. doi: 10.1007/s10461-007-9272-1. PubMed PMID: PMC2819112.
81. Tarnowski KJ, Simonian SJ. Assessing treatment acceptance: The abbreviated acceptability rating profile. Journal of Behavior Therapy and Experimental Psychiatry. 1992;23(2):101-6. doi: http://dx.doi.org/10.1016/0005-7916(92)90007-6.
82. Min Y, Agresti A. Random effect models for repeated measures of zero-inflated count data. Statistical modelling. 2005;5(1):1-19.
83. VanderWeele TJ, Chiba Y. Sensitivity analysis for direct and indirect effects in the presence of exposure-induced mediator-outcome confounders. Epidemiol Biostat Public Health. 2014;11(2):e9027. doi: 10.2427/9027. PubMed PMID: 25580387.
84. VanderWeele TJ. Mediation Analysis: A Practitioner's Guide. Annual Review of Public Health. 2016;37(1):17-32. doi: 10.1146/annurev-publhealth-032315-021402. PubMed PMID: 26653405.
85. Cohen J. Statistical power analysis for the behavioral sciences: Jacob Cohen. J Am Stat Assoc. 1988;84(363):19-74.
86. Hedges LV. Distribution theory for Glass's estimator of effect size and related estimators. journal of Educational Statistics. 1981;6(2):107-28.
87. Bauermeister JA, Golinkoff JM, Muessig KE, Horvath KJ, Hightow-Weidman LB. Addressing engagement in technology-based behavioural HIV interventions through paradata metrics. Current opinion

in HIV and AIDS. 2017;12(5):442-6. doi: 10.1097/COH.0000000000000396. PubMed PMID: 28617711; PMCID: PMC5637536.
88. Kreuter F. Improving surveys with paradata: Analytic uses of process information: John Wiley & Sons; 2013.
89. Little RJA, Rubin DB. Statistical analysis with missing data. New York: Wiley; 1987.