Trials

STUDY PROTOCOL

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Sexual Health Advocacy for Guys (SHAG): a randomized trial of the impact of a text-messaging program on HIV incidence and STI testing among a national sample of sexual minority cisgender adolescent and young adult men

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Abstract

Background Disparities in sexually transmitted infections (STI) including human immunodeficiency virus (HIV) among sexual minority boys and young men are substantial. Effective HIV and STI prevention programs that include access to pre-exposure prophylaxis (PrEP) medication do not consistently include younger sexual minority men. Text-messaging programs for HIV prevention have been associated with increases in HIV testing among sexual minority adolescent boys, but these programs have not incorporated a focus on PrEP or STIs beyond HIV.

Methods We will conduct a two-arm randomized trial with 1:1 allocation comparing the superiority of text messaging-based intervention focused on HIV and STI prevention to a generic HIV education program with content focused on promoting a "healthy lifestyle" (e.g., self-esteem). Outcomes include testing for HIV and other STIs, increasing PrEP and PEP use, and HIV incidence. Generalized linear models will be used to estimate treatment effects on primary study outcomes, with longitudinal models (estimated based on Generalized Estimating Equations) specified to examine effects over time. Mediation will be assessed based on a product of coefficients approach with bootstrapped standard errors.

Discussion This is the first randomized controlled trial (RCT) with a national sample of cisgender sexual minority adolescent boys and young men 13-22 years of age exploring the efficacy of a text messaging-based intervention in increasing HIV and STI testing, and PReP and PEP use. Findings will inform the scalability of text messaging programs for sexual health promotion and at-home STI testing, and will demonstrate impacts of a behavioral health intervention on HIV incidence.

Trial registration ClinicalTrials.gov NCT06230367. Date of registration: 1/29/2024.

Keywords Text messaging intervention, Sexual health, Sexual minority health, HIV testing, STI testing, Home-testing, HIV PReP, HIV PEP

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Introduction

Background and rationale

Sexual minority cisgender adolescent boys and young men face disparate risk for HIV acquisition: More than nine in ten new HIV infections among boys and young men in the USA are through "male-to-male" sexual contact [1, 2]. Disparities are even starker for African American/Black and Hispanic sexual minority youth, who account for 51% and 25% of new HIV infections, respectively [3]. Youth living in southern states [1] and in rural settings [4, 5] also have higher rates of HIV. While the reasons are not entirely clear, it may in part be due to reduced access to HIV counseling and the availability of preventive services, as well as less accepting attitudes towards sexual minority people. HIV testing and counseling as well as pre-exposure prophylaxis (PrEP), which can reduce one's risk of HIV up to 99% [6–11], are critical components of any comprehensive HIV prevention initiative.

In the face of all-time high STI rates across the country [12], it is concerning that youth ages 15–24 account for half of all new infections [12, 13], invigorating calls for increased prevention focus on STIs [12]. STI testing—including oral and anal tests [14]—is important because people who have non-HIV STIs are more likely to contract HIV [15–22]. This is partly due to concomitant risks (e.g., unprotected sex), but also because a sore or inflammation caused by an STI provides a pathway for HIV.

The wide adoption of text messaging provides novel opportunities for HIV prevention interventions where youth "are" across socio-demographically different groups [23], and overcomes structural challenges of traditional prevention initiatives. Moreover, being able to access sensitive content when and where one chooses facilitates safe spaces for youth to engage with the content, which is important for those who are not "out" to family and friends. Importantly too, reviews suggest that programs delivered via text messaging can affect complex behavior change, including HIV testing among sexual minority adolescent boys [24–29].

The Guy to Guy program (G2G) was the first comprehensive HIV prevention program delivered via text message to a national sample of 14–18-year-old cisgender boys who identified as gay, bisexual, and/or queer. G2G was tested against an attention-matched "healthy lifestyle" control focused on topics such as self-esteem. G2G and the healthy lifestyle control programs sent between 5 and 10 messages per day to participants over a 5-week period. At 6 weeks post intervention, participants in each program received booster messages for a week. At 90 days postintervention, there were no significant differences in either sex acts not protected by condoms or abstinence between groups. Among participants who were sexually active at baseline, intervention participants reported a threefold increase in HIV testing compared to control participants (adjusted odds ratio = 3.42, $P = 0.001$). They were less likely than control youth to be abstinent (adjusted odds ratio = 0.48, $P = 0.05$) [29].

G2G offers an example of a promising program that was implemented and tested at the national level, affording substantial reach and impact beyond traditional face-to-face initiatives for gay, bisexual, and other sexual minority cisgender adolescent boys and young men. But G2G did not incorporate a focus on PrEP, with critical information on what it is, how to access it, and when it may be indicated for use. Additionally, few studies are powered to a degree that supports analyses of HIV incidence. Given widespread availability of home testing for HIV, we now have the possibility to afford participants the privacy and convenience of a home HIV test. This has the added benefit of being able to photo-validate self-report of HIV testing while also documenting HIV incidence in a hard-to-reach audience at risk. Finally, while G2G impacts on HIV testing are important, it also is important to address common concomitant sexually transmitted infections.

In this paper, we present details on the protocol for a randomized controlled trial of Sexual Health Advocacy for Guys (SHAG), designed to test the impact of an intervention on HIV incidence and STI testing. SHAG is a text messaging-based intervention that builds on and adapts elements from multiple previously evaluated interventions, including G2G, Girl2Girl, a text messaging-based intervention focused on pregnancy prevention for lesbian and gay cisgender adolescent girls [30, 31] and In This ToGether, a text-messaging program focused on HIV prevention for Ugandan young adults [32]. SHAG is delivered via text message to sexual minority csigender adolescent boys and young men.

Objectives

Our overall objective is to estimate the effect of SHAG compared to a generic HIV education program among 13–22-year-old sexual minority adolescent boys and young men across the USA. To do so, we will first adapt content to integrate lessons learned in previous text messaging-based sexual health interventions, as well as to include information on PrEP and PEP, and add messages that are more age-appropriate for sexually active young adult men. Next, we will demonstrate the feasibility of using OraQuick home tests to collect HIV test results via photo-verification among this age group. Finally, we will test the impact of SHAG on each of our primary study outcomes (1) HIV incidence, (2) self-reported PrEP and PEP use, (3) HIV status, and (4) number of STIs in the past 12 months.

Trial design

This will be a two-arm randomized controlled trial with a 1:1 allocation ratio comparing the superiority of exposure to SHAG versus an attention control condition.

Secondary outcomes include (1) information about and (2) motivation for uptake of PrEP; (3) STI testing; and (4) the impact of the intervention on mental health indicators.

Methods: participants, interventions, and outcomes

The following is presented per the Standard Protocol Items: Recommendations for Intervention Trials (SPIRIT) Reporting Guidelines [33].

Study setting

The SHAG intervention is designed for delivery via text message to people across the USA who own their own cell phone and are enrolled in unlimited text messaging plans.

Eligibility criteria

Eligibility criteria are meant to result in a study sample that approximates young people who would be most likely to take part in the intervention if it were publicly available. Thus, youth will:

(a) Have been assigned male sex at birth and currently have a cisgender identity,
(b) Be aged 13–22 years old,
(c) Have had anal sex in the past 12 months,
(d) Be English-speaking,
(e) Exclusively own a cell phone with an unlimited text messaging plan and intend to have the same cell phone number for the next 6 months,
(f) Have Internet access to complete online surveys,
(g) Provide informed assent for those under 18 and consent for those 18 years of age and older, including a capacity to consent [34] and a positive self-safety assessment [35],
(h) Willing to take an OraQuick home test to confirm HIV negativity for youth who are 19–22 years of age or 18 years old and graduated high school. If they agree to do the test but do not upload a photo of their result, they will be eligible if they self-report a negative HIV serostatus.
Youth 18 years old who have not graduated high school and youth 13–17 years of age will be given the option to take a home-based HIV test. If they determine that they cannot do so safely, they will be allowed to self-report their HIV serostatus; and
(i) Not be currently enrolled in another HIV prevention program or know anyone already enrolled in the SHAG RCT.

Justification for these criteria

(1) Both our own experience and other national data show that low-income youth are as likely as higher income youth to have unlimited text messaging plans [36]. Only 2% of screeners in Girl2Girl were ineligible because they did not exclusively own a cell phone with an unlimited text messaging plan. We believe text messaging increases access to the intervention rather than reifies the impacts of the digital divide. (2) We include all recently sexually active youth irrespective of whether they have used condoms because HIV incidence rates are based upon all sexual minority boys—not just those who report recent unprotected sex. (3) We include 13-year-olds to address gaps in HIV prevention for younger audiences. (4) Most Hispanic youth speak English; therefore, we believe that delivering the intervention in English will still be inclusive [37]. (5) Finally, we exclude friends of those already enrolled because of potential contamination if one is randomized to the intervention and the other to the control arm.

Gender diverse youth will be excluded because the necessary tailoring of content that is appropriately gender affirming and speaks to the unique factors impacting gender diverse youth's HIV preventive behavior is incredibly important and also beyond the scope of the current study.

Determining co-enrollment of study participants in other clinical trials

We will rely on self-report of current participation in other clinical trials. In previous RCTs, we have found that when asked, youth will tell us without hesitation if they were referred by a friend into the study. This is because we do nothing to suggest that they have done something "wrong." We anticipate similar disclosure for both questions in the current trial.

We will ask youth who indicate they are part of another clinical trial, the name of the HIV prevention program. We will use this information to endeavor to find information about the trial online. If we cannot find the program online, we will contact the youth and ask the youth to describe the program in detail. It may be that the program has not been registered online (e.g., in ClinicalTrials.gov); or that youth appraise it to be a clinical trial but it is not (e.g., maybe they are doing a survey but it is not an intervention). One example of an intervention that would meet exclusion criteria is "Hey Friend," as registered on ClinicalTrials.org (https://clinicaltrials.gov/ct2/show/NCT04846946?recrs=ab&type=Intr&cond=Hiv&cntry=US&gndr=Male&age=0&draw=2&rank=2).

Who will take informed consent / assent?

We have obtained a waiver of documentation of informed assent/consent so that a verbal or clicked "yes" will be sufficient; a signature will not be required.

Obtaining informed consent

For those who are 18 years of age and older and not in high school, the consent will be self-administered via an online website. This includes a self-safety assessment with graphics to encourage participants to think through different scenarios that could potentially place them in danger (e.g., a partner intercepts text messages about anal sex). They also will complete an automated capacity to consent, which queries whether the person understands their voluntariness, the risks of participating, etc. If the person indicates that they may not be safe, they will be encouraged to not take part in the study. Those who have questions about the study or want to confirm that it is a "real" research study will be encouraged to reach out to study staff via text message, email, or phone.

The self-enrollment website will be developed in Year 1 of the grant and function very similarly to the self-enrollment website we have used for Girl2Girl, including the automated self-safety assessment [30, 38].

Obtaining informed assent

We have obtained a waiver of parental permission for participants under 18 because requiring parental permission could increase risk to participants who may be victimized by their parents because of the need to disclose their sexual minority status. A waiver also is necessary to avoid fatal sampling bias that would occur by only including youth who are out to their parents.

The research staff, all of whom are trained in Human Subjects Protections, will discuss over the telephone assent information with the candidates who are 17 years of age and younger, or those who are 18 years old and still in high school. The participant will be asked to complete a brief capacity to assent assessment, which will measure his ability to understand the potential risks of participation [39]. Specifically, participants will be quizzed to assess their capacity to understand, appreciate, reason with, and express a choice about participation using a modified version of the Evaluation to Consent Form [34, 39, 40]. Modifications involve the specific risks that could result from participation (e.g., "If someone sees one of the project texts, they may ask me about my sexual identity"). Participants who do not demonstrate a capacity to assent will be ineligible.

Given the high rates of interpersonal victimization that sexual minority youth report [41], we believe that children who are eligible for this study will be well equipped to self-assess their safety, as they have to do so every day of their lives. Study staff will complete a self-safety assessment with the potential participant that includes discussion of different possible scenarios and asking them whether they feel safe in each situation. This conversation will include concrete examples, such as their caregivers monitoring their cell phone use and text message content. If the participant is hesitant at all, he will be advised not to participate. While this protocol will likely result in fewer participants assenting, it will result in a safer cohort. The sample also will be more reflective of the actual end user. While it may be uncommon to empower youth to make their own safety decisions, this self-safety assessment was used successfully in Guy2Guy, Girl2Girl, and In This toGether.

All participants will be given the opportunity to ask any questions. A link to the assent / consent form will be sent via email for his later reference, should he request it. [Some youth may not desire it be sent for safety reasons.] Phone numbers for the Principal Investigator (PI) and the Institutional Review Board (IRB) will be listed in the assent/consent forms and on the intervention website, in case a participant has a question or would like to discuss the study or any concerns.

Additional consent provisions for collection and use of participant data and biologic specimens

Home-based HIV tests

During enrollment, older youth will be asked to think how to safely receive the mailed home-based HIV test. Younger youth who chose to receive a home-based test will be asked to think about the same.

If it is safer for youth to have the package mailed to an address other than their home (e.g., because a parent may question what is inside), we will send it to another address that they specify. We will send the USPS tracking information to participants so that they can opt-in to real-time tracking of when the package is going to be delivered and are empowered to redirect the package should they need or want to. If young adults are not able to identify during enrollment a place where we can safely mail to them the package, we may offer the option of mailing the test to an Amazon Hub Locker. In these instances, the test will be purchased and mailed by Amazon. Younger participants (i.e., those who are 13-17 years of age or 18 years of age and still in high school) who do not think they can receive or do the home-based HIV test safely may opt out.

Interventions

Explanation for choice of comparators

Text messaging interventions and other interventions that rely on technology solutions design attention control comparators to ensure that observed effects can be

Table 1 Example SHAG messages

HIV Information	Lube also reduces the chances that the fragile skin around the anus and in the rectum will tear. It also keeps the condom from breaking (see how I worked that in there? ☺)
	PrEP is a pill you take every day or a shot you get every 2 months. It reduces your risk of HIV by 99% (for real) when you take it the right way.
HIV Motivation	I know it may feel like the 2000s to talk about HIV, but the truth is: Among people who are living with HIV, 2 in 3 are guys who are into guys. This is real. It affects all of us.
HIV Behavioral Skills	Maybe trusting doctors is hard – not all doctors are LGBT+ friendly. Here's a website with doctors who have experience working with LGBT+ folks: lgbtqhealthcaredirectory.org. Finding a doctor now might help when you need one in the future.
	You might tell your partner that you've learned stuff in SHAG - like how great PrEP is at preventing HIV, and condoms are at stopping STIs; and that testing every 3 months is important just to be safe. You want to follow this plan.
	It's perfectly ok to start doing something even after you've stopped – or never done it. Every time you have sex is a new chance to make a healthy decision.
Socio-cultural factors	Violence is *never* ok. If there is violence in your relationship, you might feel like you're the only one going through this, but remember: You are not alone.

appropriately attributed to intervention content rather than to the benefits of receiving messages only.

The comparison group in this trial will receive a similar number of text messages for the same number of days as the intervention group. The content for the comparison group will focus on generic HIV prevention education and other healthy lifestyle topics (e.g., moving your body, self-esteem). Dyadic messaging features included in the intervention to increase program engagement are not included in the control content.

Intervention description

Intervention messages will be conversational in tone and build upon each other daily and weekly throughout the intervention. "Core" content will be delivered across ~8 weeks. Between 8 and 15 program messages will be sent each day. Although this may seem like a lot, half of teens send 60 text messages a day [42], which is likely why we have found this intensity to be acceptable to young people [43, 44].

As shown in Table 1 below, messages targeting motivation to engage in HIV preventive behaviors discuss the importance of HIV testing and not assuming a partner's sero-status, and normalize the idea that condom use is a loving way to show that you care about your and your partner's health. Behavioral skills include messages about how to talk to a healthcare provider about PrEP and PEP, and how to talk to one's partner about using condoms. Content will discuss the benefit that PrEP can have if having condomless sex is one's current reality, and how PEP can be used if a single unprotected sex act happens.

We also will link to brief videos where visual information is critical to achieving the learning objective. For example, messages that discuss how to use a condom are complemented with embedded links to interactive demonstrations.

Criteria for discontinuing or modifying allocated interventions

There are no specific criteria to modify the control or intervention arm content, but we do recognize that external events may warrant consideration of new content or adaptation of existing content. For example, during the COVID-19 pandemic, we made changes to Girl2Girl content that seemed to be exacerbating mental health issues for some who were particularly stressed by the pandemic. Although we do not anticipate something similar, it may arise. In this case, we will document any changes made to content and work to maximize fidelity throughout the trial.

Participants can self-select to discontinue their participation at any time; in these instances, data collected up to the time of discontinuation will be retained for analysis.

Strategies to improve adherence to the intervention

Personalizing the content increases the self-relevance of material, thereby improving the likelihood that the information will be understood, remembered, and produce behavior change [45–47]. Examples from previous research demonstrate that content can be written for different "paths" that present the same concepts but in ways that are more relevant to specific subpopulations (e.g., those who are having sex with guys versus those who are having sex with guys and women). We will explore the possibility of creating paths to tailor content, for example by racial/ethnic identity and urban/ rural settings. Youth will also have opportunities to tailor the program to their daily schedule. They can determine when the messages start and end each day, which ensures that they will be sent at appropriate times (e.g., after band practice) and therefore will be more likely read. Participants also will determine the intensity of their messaging: A longer window of messaging means that the messages will be more spaced out across the day.

Promoting program engagement using bi-directional messages: There are several features that use bi-directional messaging to increase the interactivity of the intervention, which in turn, we posit will promote adherence to the intervention. These include offering "Text Buddies", i.e., pairing participants with others in the program that they can communicate with via text for the purpose of practicing newly acquired communication skills [48]; "gamifying" content, a strategy demonstrated to increase engagement with and commitment to an intervention [49] with elements such as points and leveling up to more challenging content; and opportunities to earn badges to demonstrate competency of HIV preventive behavioral skills.

The intervention will link to a screening tool that will help youth better understand their HIV risk and to identify preventive options that best fit them.

Relevant concomitant care permitted or prohibited during the trial

Potential participants are not eligible for SHAG if they are currently enrolled in other HIV prevention programs or if they are HIV positive at baseline. People who seroconvert during the RCT will be encouraged to access care and will be able to remain enrolled should they so choose. Everyone will be encouraged to talk with a medical provider about PrEP and whether it is a good fit for them.

Provisions for post-trial care

As a behavioral health study, we do not anticipate physical harm because of the study and so do not have provisions for compensation or post-trial clinical care. Youth will be provided referrals to other organizations throughout the study should they want to continue to engage in healthy sexuality discussions and related care.

Outcomes

Measures for outcomes of the RCT

Because PrEP is an outcome, providing it as part of the study would negate the possibility of measuring the intervention's impact on its uptake. The primary and secondary outcomes are as follows:

Primary outcome measure

HIV Incidence determined by home testing kit.

[Time Frame: 12-month post-intervention and immediately post-intervention].

Secondary outcome measures

2. Self-reported HIV incidence

[Time Frame: Post-Intervention, 3-month post, 6-month post, 9-month post, 12-month post]

3. Proportion of participants testing for an STI

This outcome will be measured as a cumulative indicator of whether the individual has tested for an STI

[Time Frame: 12-month post intervention and immediately post-intervention]

4. Proportion of participants having used PrEP/PEP

This outcome will be measured as a cumulative indicator of whether the individual has used pre-exposure or post-exposure prophylaxis for HIV

[Time Frame: 12-month post-Intervention and immediately post-intervention].

Participant timeline

We have allocated at least 27 months for participant enrollment. After enrollment, young adults, and children who opt in, are mailed an OraQuick home-based HIV test by Molecular Testing Labs (MTL)—see "Confirming HIV sero-status" below.

We will reach out to those who are ineligible because of a positive HIV test to link them to local resources and encourage them to seek a confirmation test and counseling, we will email candidates who are ineligible for other reasons referrals and resources. This lag is to reduce the likelihood that they will return to the screener to try to enroll again but with different answers.

Confirming HIV sero-status

We chose OraQuick over a dried blood spot, which is more accurate, because we anticipate a higher response rate with the home-based test. For example, in one study where 15–24-year-olds were able to order OraQuick home-based HIV tests, 65% ordered it, 75% of whom self-reported using the test during the course of the study [50]. In the current study, youth are being proactively sent the HIV test rather than ordering it; as such, we anticipate the 75% marker to be relevant and anticipate that 75% of those who are assented/consented will complete the test a baseline.

We will send the baseline online survey to those who are getting a home-based HIV test mailed to them on the day the test is received (we will be able to track the test delivery by using the USPS tracking number provided by MTL). Participants will be told to take a picture of the HIV test result and upload it to the survey platform. If the photo is unreadable, we will ask the participant to upload another picture. If the test is inconclusive, we will ask the participant to go to a local clinic for a confirmatory test. If the HIV test is positive, we will provide resources for the participant to link them to care locally. Those who decline to upload a photo of their test may self-report their sero-status.

Once we have confirmed receipt of a photo of the HIV test and that it is negative, the participant will be randomized and program messages will begin. The testing procedure will be similar at intervention end and 12-month follow-up.

The tests will be mailed in non-descript packaging so people handling the box will not know what it contains. We will send the tracking information to participants if they request to receive it so that they will know when the package is going to be delivered and are empowered to redirect the package should they need to review instructions that are included with the test.

Intervention length

The total intervention length will be about 5 months. After the ~8-week "core" messaging period, participants will enter a 12-week "latent period" during which they will receive 2–4 messages per week that encourage them to integrate their new HIV preventive behaviors into their everyday lives. The intervention will end with a 1-week "booster" session that reviews fundamental intervention topics. Messages will highlight key messages presented in the 8-week core content. Results from other trials suggest that this latent period may be particularly important in enacting behaviors that require a healthcare provider (e.g., PrEP acquisition) [30, 31, 38].

Assessment timeline

Participants will complete seven surveys: At baseline, "core" intervention end, and intervention end; and 3-, 6-, 9-, and 12-month post-intervention end. Sero-prevalence via home-based HIV tests will be measured at baseline, intervention end, and 12-month post-intervention end. We choose these time points to measure proximal (i.e., intervention end) and distal (i.e., 12 months post-intervention) impacts of the intervention on incidence. At all other time points, youth will self-report whether they have been tested since the last survey, and the outcome of the test. To maximize data, participants will be invited to complete each survey irrespective of whether they completed the previous survey.

Study timeline

At least 27 months will be devoted to recruitment; follow-up data collection will occur through 12 months post-intervention end for participants. The total observation period will be 17 months: 2 months for the "core" intervention, 3 months for the latent period and review week, and 12 months of follow-up. This results in an almost 4-year field period. Data analysis will occur in year 5.

A timeline conforming to the SPIRIT guidelines can be found in Fig. 1.

Sample size

The proposed sample size for the current study is $N=5000$ youth. We conducted power analyses to determine whether the proposed sample size is adequate to test the intervention's impact on reducing self-reported HIV incidence (primary study outcome). We focused on this outcome measure because it is the least common of the main outcomes identified. As such, if we have sufficient power to detect HIV incidence, we have sufficient power for testing the effect of SHAG on all other primary study outcomes.

Effect sizes for the power calculation were based on prior work. In a study of 450 men who have sex with men aged 16–20 years old, Garofalo et al. reported the 12-month HIV incidence rate to be between 2.0 and 6.0, with 95% confidence [51]. To be conservative, we assumed a 30% loss to follow-up, which is considerably higher than we have seen in previous studies by this research team. Given that we are interested in determining whether the intervention has a positive impact, a one-sided alpha level was specified. Results using PASS Sample Size and Power [52] suggest that using a log-rank test we will have power = 0.8 to detect a hazard ratio ≤ 0.5 implying a difference between the HIV incidence rates in the treatment (SHAG) and control if the population HIV incidence rate is 2% or higher, with a p-value of 0.05 or less.

Recruitment

Participants will be recruited primarily through social media and dating applications. We have had success in prior research in recruiting large numbers of sexual minority youth via social media. Instagram (IG) is one of the most popular online platforms adolescents use, although low-income teens are more likely to use

	STUDY PERIOD							
	Enrolment	Allocation	Post-Allocation					
Timepoint	-t1	0	Months 1-2	Months 3-5	Month 3	Month 6	Month 9	Month 12
Enrolment								
Eligibility screen	X							
Informed Consent	X							
Allocation		X						
Trial								
Intervention			X	X				
Control			X	X				
Assessments								
Demographics, text messaging characteristics		X						
Main Outcomes: HIV/STI incidence, PEP, PReP uptake		X	X	X	X	X	X	X
Secondary Outcomes: Sexual risk behavior & context, STI Testing, Coming Out, Violence, Substance Use		X			X	X	X	X
Other Variables: Exposure to other HIV interventions		X			X	X	X	X

Fig. 1 SHAG study timeline per the SPIRIT guidelines

Facebook (FB) [53]. Because FB owns IG, ads run on both platforms, ensuring wide visibility and reach across different groups of young people.

We do not ask youth to refer their friends because this has the potential to create problems with randomization (i.e., if one is randomized to the intervention and the other to the control).

Given the increased vulnerability and therefore need for protection of children under 18 years of age, we have two enrollment strategies, based upon age:

- All youth who view the IG / FB ad and want to learn more will click on it, linking them to the project website. There, they read a description of the study activity and, if interested, complete an eligibility screener. Participants are not required to register to complete the screener; this step is similar to a contact form.
- Those who are older, defined as being 19–22 years of age or 18 years of age and not in high school, and eligible will go on to enroll themselves online by completing an automated self-safety assessment and agreeing to the informed consent document and capacity to consent survey.
- Those who are younger, defined as being 13–17 years of age or 18 years and in high school, will have an enrollment telephone call with research staff to go over the assent, capacity to assent, and self-safety assessment together.

About 27 months will be devoted to recruitment. As noted above, we anticipate about 75% of those who assent/consent to take part will provide baseline HIV testing results. If accurate, then we will need to consent/assent 6667 young people to randomize 5000. To meet this goal, we will need to enroll ~ 100 youth under the age of 18 each month. If we are not receiving a sufficient number of screeners, we will work with our research team and young people to gather ideas about how to better target younger youth.

We anticipate ~ 150 youth 18–22 years of age self-enroll each month. [We anticipate about two-thirds of the sample will be older because older adolescents have sex more frequently than younger adolescents.] If enrollment rates for older youth are lower than anticipated—especially because they are being asked to complete an HIV test without talking with a live person on the telephone, we will conduct phone outreach to people

who have submitted eligible screeners but have not yet enrolled to invigorate rates if need be.

Ensuring diversity

Half of gay and bisexual men who are HIV positive are Black or African American, as are 25% of sexual minority Latinx men [3]. As such, it is vital from a public health perspective to ensure that racial and ethnic minority youth are well-represented in the study. Additionally, almost one in five people who are HIV positive live in rural areas [54]. Social media is particularly amenable to achieving sample diversity because we can target ads on youth characteristics. We may also reach out to social media influencers from these harder to reach populations to promote the study. To endeavor to have at least 50% of the sample is Black/African American, Latinx, and/or mixed race, and 20% are living in a rural area or southern state, we will impose diversity targets during the enrollment process. Once we have randomized the target number of youth from a particular "bin" (e.g., White, non-Hispanic), all subsequent youth from this group will be ineligible.

Assignment of interventions: allocation

Sequence generation

The randomization allocation table was generated based on a permuted block randomization procedure with small, random-sized blocks. Randomization was stratified by age (younger [defined as 13–17 years of age or 18 years of age and in high school] /older [defined as 19–22 years of age or 18 years of age and not in high school]) and sexual identity (gay/bisexual), ensuring equal allocation across age/education x sexual identity subgroups. The randomization sequence was generated by the study statistician and monitored by the PI.

Concealment mechanism

Randomization assignment will be automated using a 4-, 6-, and 8-block randomly alternating design programmed by software developers. Researchers will not have access to the algorithm. Only the software developer and biostatistician will be able to view the assignments in the data.

Implementation

Youth will be enrolled sequentially within the stratification group (or "bin"). Once a "bin" is full (e.g., White non-Hispanic urban), no other people who have the same profile will be eligible. Older youth will enroll themselves online. Younger youth will be enrolled over the telephone by research staff. Participants will be randomized after they are enrolled and complete the baseline survey.

Assignment of interventions: blinding

Who will be blinded

Participants are blinded to their assigned study arm; there is no blinding of the research staff to the intervention or control arm.

Procedure for unblinding

We will communicate to participants the arm to which they were assigned once all data collection has been completed.

Data collection and management

Plans for assessment and collection of outcomes

The measures planned for collection are identified above. Participants will upload documentation of home-based HIV test results and self-administer surveys online. Participants will key in their own data through online surveys. Variables will have validity checks such that out-of-range answers (e.g., condom use greater than the number of times one has had sex) will be disallowed. Data will be reviewed (blinded to treatment assignment) on an ongoing basis to assess quality and completeness.

Plans to promote participant retention and complete follow-up

Incentives

Incentives are commensurate with those used in previous studies of sexual and gender minority (SGM) youth [29–31] and are purposefully nominal so that they are not coercive. Youth in the RCT will receive graduated incentives over time: $15 for the intervention end survey and $25 for each follow-up survey except for the final survey, which they will receive $30 for completing.

For older youth as well as younger youth who chose to do an HIV test, they will be incentive an additional $30 for uploading the OraQuick test result at baseline, $45 at intervention end, and $60 at 12-month post-intervention end.

We may also offer an "early responder" incentive of an additional $5 for those who complete the follow-up surveys within the first 72 hours. .

Based on prior research, some SGM youth prefer not to receive an incentive for reasons of safety. As such, participants will have the option to choose to receive their incentive amounts as an Amazon gift card emailed to them, as a donation to a charity, or neither. They will not be otherwise compensated for their participation. Participants will not incur additional costs to take part in the study beyond what they already pay for Internet and text messaging.

Survey reminders

To increase initial enrollment rates, participants will receive automated and then personalized outreach to encourage the sending of one's HIV test results, and to complete survey assessments.

Inviting all youth to complete the next survey follow-up irrespective of previous non-response

To maximize data, participants will be contacted at each data collection period irrespective of their participation in prior follow-ups, unless they have withdrawn from the study. Participants who do not complete the online surveys within 1 week may be given the opportunity to complete a brief text message survey for a smaller incentive amount. This methodology has been successfully implemented in our previous studies. Indeed, this brief survey can sometimes serve as a gateway to the full-length survey for non-responders [55].

Constantly updating contact information

We anticipate we will be able to stay in contact with youth throughout the 15-month study period (i.e., 5-month intervention + 12-month follow-up). In our previous studies, we have found social media to be particularly useful in re-connecting with participants and updating their contact information and will similarly plan to use social media to stay in contact with participants in the current study.

Fidelity monitoring

Text messaging is associated with high fidelity because everyone receives the content in the same order; whereas in-person programs are subject to the facilitator's choices about what and when content is discussed. It is possible that unexpected technology problems may affect the sending of the messages. To quickly identify and address such problems, we will monitor project messages daily.

Retention strategies

To increase initial enrollment rates, participants will receive automated and then personalized outreach to encourage the sending of one's HIV test results. We anticipate a 70% test confirmation rate at intervention end and 12-month follow-up. We anticipate an 80% response rate to each online survey, consistent with prior work [29].

Data management

Missing data

The primary anticipated reason for missing data is attrition due to loss to follow-up, however, also may occur within a case (skipping certain questions). This includes those who complete a self-reported follow-up survey but do not upload a photo confirming the result of their OraQuick home-based test at either intervention end or 12-month post-intervention follow-up. Our statistical methods will employ full-information maximum likelihood or incorporate the expectations-maximization algorithm so that all randomized individuals can be included in an analysis even if they are lost to follow-up and/or have partial missing data. These methods are robust to data that are missing at random [52, 56].

We will conduct sensitivity analyses to contextualize how assumptions about the missing data mechanism influence our understanding of intervention impact. To do so, we will follow recommendations made by Leacy et al. [57] and also analyze data with missing data coded as failure and with missing data coded as success.

Confidentiality

Safe and private data collection

We believe that delivering content directly to young people' cell phones creates a more private "space" than other types of programming (e.g., those which are delivered in-person).

To protect participants' privacy, RCT data will be collected via online surveys. This reduces the number of people who view the data and increases self-disclosure on sensitive topics. We will password protect access to the data. We will ask youth to upload a photo of their HIV / STI test to the secure online survey platform and encourage them to delete the photo from their phone afterwards (see "Secure Electronic Transmissions and Storage of Data" below for more information).

Participants will access surveys with a personalized link. Dr. Ybarra will oversee data collection, with the project coordinator coordinating with the software developers and biostatistician to continuously monitor the data.

At any time during the online surveys that participants are asked to complete, they will have the option to pause or stop the survey and return to it at a later time (i.e., if they choose to provide an email address, we will send them a link to re-enter their specific survey). We will emphasize to the respondent that this option can be utilized if he feels that the space where he is completing the survey is no longer private.

At the beginning of each survey, we also will ask survey respondents: (1) Are you in a space that feels private? and (2) Are you in a place where you feel comfortable answering questions honestly? Those who say "no" to either question will be advised that taking the survey somewhere private and safe is important. They will have instructions on how to pause the survey and resume it later if they would prefer.

Data privacy

We will assign each participant a random unique identifier in the dataset, stripped of all personal information to protect confidentiality. Datasets used for analysis will contain project identification numbers, but not names or any other identifying information such as phone number or email address. We store identification information separately from the responses provided by participants.

Collaborators will receive data stripped of personal identifiers. To ensure complete confidentiality, we will restrict access of the key linking personal identifiers to usernames and passwords to main program staff. Dr. Ybarra will oversee the data storage and reporting procedures. Reports will not identify individual participants; they will only use aggregated data.

It is possible that participants may lose their confidentiality if someone intercepts their phone. Study staff will offer instructions to participants on how to password protect their phones to limit access by others. Staff will also encourage participants to disable text message notifications that may appear on a phone screen and to delete any messages from their phone that they do not want anyone else to see.

Participants may lose their confidentiality if someone intercepts the shipping box that has their HIV test, or the HIV test itself. We will encourage youth to have the package mailed to a safe place, including the address of a friend or family member if necessary. They also will be given the tracking information so they can divert the package if need be. We also will remind people to safely and securely dispose of the test once they have uploaded a picture to the online survey platform (e.g., the survey thank you message will encourage them to do so).

No additional contact information (e.g., additional phone number, friend's number, physical address) beyond their cell phone number and email address will be required to enroll. Participants will only provide additional contact information if they choose to and can do so safely. Our team has extensive experience using this contact information in a manner that is sensitive to the privacy needs of youth participants.

Secure electronic transmissions and storage of data

Data are located on dedicated servers at both Digital Ocean and Liquid Web data centers. Both data centers provide strict security compliance ensuring both physical and network security. Both servers are continuously monitored to ensure 100% uptime.

The dedicated server facility security includes:

- 24/7/365 Manned Facilities
- CCTV Security Cameras Covering Inside, Outside and All Entrances of Data Centers
- Site Entrances Controlled By Electronic Perimeter Access Card System
- Sites Remotely Monitored By 3rd Party Security Company
- Entrances Secured by Mantraps with Interlocking Doors
- SSAE-16 & HIPAA Compliant, Safe Harbor Certified

The data centers are equipped with redundant tier 1 bandwidth, ensuring minimal latency and fast connections to all points of the global Internet. Datacenter access is strictly limited to technical staff. Electronic security systems control datacenter access and are accompanied by a full complement of motion-detecting security cameras that monitor the entire facility.

All data are password protected with strong encrypted passwords and is transmitted securely using SSL (TLS) 128-bit encryption across the Internet (HTTP). SSL provides front-end users with the assurance of access to a valid, "non-spoofed" site and prevents data interception or tampering with sensitive information. The 128-bit encryption is the preferred security level of government and financial institutions. To ensure against the remote possibility that an intruder gains access to stored data, all data stored are protected with strong passwords that are also encrypted, making use of any acquired data nearly impossible. Any Personal Identifying Information (PII) is securely encrypted and stored separately from study data. All access to participant data is limited to access via a secure VPN network, making it impossible to access otherwise.

Our data are backed up daily to an external hard drive. We also have extensive server-hardening, firewall protection, brute force detection and evasion, denial-of-service attack prevention/protection, and conduct daily security audits and monthly vulnerability scans.

Plans for collection, laboratory evaluation, and storage of biologic specimens for genetic or molecular analysis in this trial/future use

The HIV test specimens are self-collected by participants who are using the OraQuick diagnostic test. The test is self-administered and results are available to users at the point of specimen collection within 20 min of completing the test. Participants will be asked to self-report their results by uploading a photo of the test. Only those that are unreadable will be confirmed via laboratory result at a local health clinic unaffiliated with the study. Each individual test taker will dispose of their test and testing components per OraQuick instructions. Thus, we have no plans to conduct laboratory evaluation, and/or store specimens for any current or future use.

Statistical methods

Statistical methods for primary and secondary outcomes

Our primary analyses will be based on the intention to treat (ITT) principle, with all randomized participants included in the analyses regardless of the amount of data they contribute. Analyses will be based on the initial treatment assignment and not on the treatment eventually received.

Main outcome: OraQuick-confirmed HIV incidence

We base our choice of when to measure HIV incidence using OraQuick home-based tests so that we are able to measure proximal (i.e., intervention end) and distal (i.e., 12 months post-intervention) impacts of the intervention on incidence. Distal impact will be our main analysis of interest.

To do so, we will utilize Kaplan–Meier survival analysis and the log-rank test of differences given experimental arm assignment through the 12-month post intervention end. In survival analysis, we are interested in estimating two systematically related probabilities: the hazard probability (HP) and the survival probability (SP). In a discrete-time framework, HP is the ratio of individuals who report, for example, a positive HIV test at a particular time point divided by the number of individuals who were at-risk and did not report a positive HIV test at the prior time point. SP refers to the probability of an individual surviving at least until a given period without reporting a positive HIV test, given that he has survived the earlier time period. Both probabilities can be plotted to provide information about periods of greatest risk over time. The DTS model is particularly amenable to incidence analyses as it can appropriately account for censoring individuals after they drop out of the study prior to 12-month follow-up (i.e., right censoring).

If treatment (treatment = 1, control = 0), were estimated to have a hazard probability of 0.5, we would say that the likelihood of an incident HIV test at intervention end for the intervention group was half the probability of a positive HIV test among the control group. In secondary analyses, we will us cox-proportional hazard models to explore the potential impact of the following baseline variables: age, race, ethnicity, region of the country, sexual identity, history of HIV and STI testing and PrEP use.

We will examine potential mediators of the treatment effect on the primary study outcomes such as motivation to use PrEP. We will test mediation using a product of coefficients approach with bootstrapped standard errors (10,000 bootstrapped samples). This will allow us to estimate path coefficients: a path (effect of treatment assigned on changes in PrEP motivation), b path (effect of PrEP motivation on HIV incidence) and their product a*b (indirect effect of treatment on HIV incidence through PrEP motivation).

To understand how program components may impact the targeted outcomes, we also will examine whether program appraisal, program dosage, and process measures are associated with the intervention impact on HIV incidence among intervention participants.

As a planned secondary analysis, we will estimate the log-odds of the intervention impact on confirmed HIV incidence at intervention end. This will inform whether difference in incidence was detectable more proximally.

Main outcome: self-reported HIV incidence

In addition to test-confirmed HIV incidence, we will collect self-reported HIV incidence at all time points. This will maximize the amount of data we are collecting on this measure and will give us an opportunity to examine the impact that self- versus test-confirmed results impact the conclusions we draw about intervention impact. The self-report outcome will include data from all post-randomization assessments.

Figure 2 shows a comprehensive discrete survival model which includes regression paths for direct effects (X, Y), moderation effects (X*Y), and mediating effects (M). We will use generalized linear models with a logit link to examine the effect that covariates have on the timing of the positive self-report parameterized by its effect on the log hazard odds of an event during a given time interval. Thus, a covariate's effect on the likelihood of event occurrence is described in terms of the hazard odds ratio (hOR).

Constraining covariate effects to be time-invariant will make the effects on the hazard probability identical for each time interval. In other words, the hOR is constant over time (i.e., proportional hazard odds assumption). When this constraint is relaxed, the covariate effects are permitted to be time-variant. For example, a time-variant effect of treatment status indicates that the odds of a positive self-report in the intervention compared to the control group changes over time. As with test-confirmed HIV incidence, we will test effect moderation for self-reported incidence using interaction terms (e.g., race X experimental arm) and mediation using the product of coefficients approach, as above.

Assessing the relative benefit of biological outcomes versus self-report

There is an assumption that biological outcomes are needed to identify the "true" impact of an intervention because of inaccurate self-reporting. Based upon research in other areas [58, 59], there seems to be little reason to believe that there would be differential reporting by arm

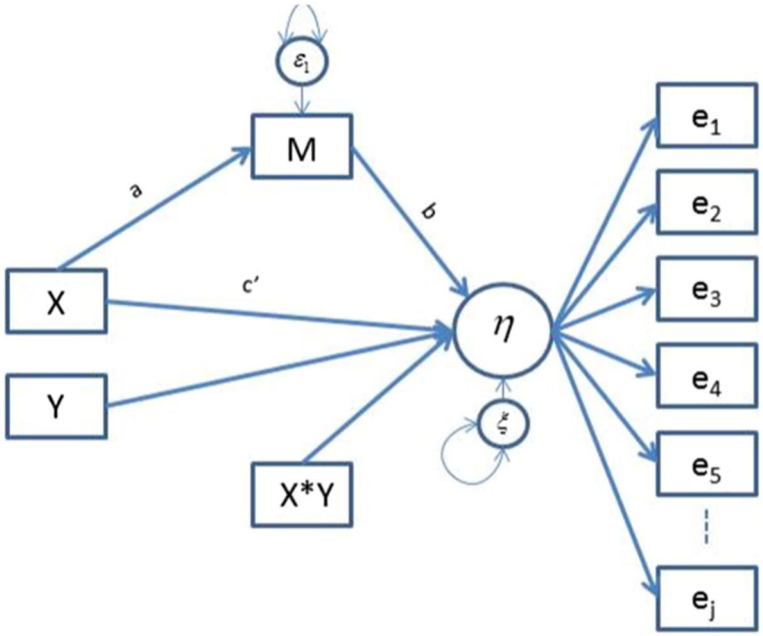

Fig. 2 Planned SHAG analysis: discrete survival model

(i.e., that the intervention arm would be less likely than the control arm to report an observed positive test)—especially in interventions such as Project SHAG where participants are blinded to their study arm. If true, we would expect the relative magnitude of intervention impact to be the same for test- and self-reported HIV status. Perhaps, however, people tend to over-report their test results when self-reporting and the test-confirmed report is a more sensitive measure. If true, then we would expect the actual intervention impact to differ for the test- and self-reported HIV status. We will explore interrater reliability between self-report and OraQuick results across arms.

In addition, we will calculate levels of interrater agreement (kappa) to quantify agreement between self-report and lab report at intervention and study end. We will use multinomiallogistic regression modeling to explore associations between participant characteristics and discordance between self-reported and OraQuick confirmed HIV incidence with 3 outcomes: (1) OraQuick-confirmed and not self-reported, (2) self-reported and no OraQuick report, (3) OraQuick-confirmed and self-reported.

Main outcome: number of self-reported STIs

Because participants can have a positive STI result more than once either for the same or a different type of STI [60, 61], we will use a count regression approach to model the impact of the intervention on STI infections over time [62]. Using generalized linear mixed models with a log link function and Poisson distribution, the model will estimate the incident rate ratio for STI infections for those in the intervention versus control group. A random effect for individual will account for the repeated measures throughout the study. If assumptions of the Poisson model are violated (e.g., overdispersion), a negative binomial model and if necessary zero-inflated models will be considered as alternatives. We will also conduct mediation and moderation analyses as described above.

Main outcome: pre-exposure prophylaxis (PrEP) / post-exposure prophylaxis (PEP) uptake

We will evaluate intervention impact on PEP/PrEP uptake using generalized linear mixed models using a using the binomial distribution and logit link function. These models will include random effects to account for repeated measures within individuals, as above. Utilizing the 7 data collection timelines, including baseline, models will (1) characterize the temporal trend of PrEP/PEP use between baseline and 12-month follow-up, and (2) assess whether these trends vary by intervention status. Mediation and moderation will be explored as described above.

Interim analyses

Monitoring of Text Buddy communication

Text Buddies are intervention participants whom we will pair together and encourage to talk to each other about program content throughout the intervention. We posit that practicing new behaviors with a Text Buddy will reinforce HIV preventive behavior change over time.

However, balancing this with the privacy needs of our participants, who likely will not want a person unknown to them to have their cell phone number, is important. To achieve this, all Text Buddy messages will be routed through the study server, replacing the need to exchange cell phone numbers. Buddy conversations will be saved in a password-protected file. For analysis, we will keep a count record to reflect the number of messages sent by each participant.

We will have a safety plan for Text Buddies. It is possible that interactions between Text Buddies will be unhealthy (e.g., encouragement of risky sexual behavior). We will monitor the interactions between Buddies daily during the RCT to determine if this occurs. We also will block messages that contain key words (e.g., contact information) for review before they pass through to the Buddy. *Any concerning message content will be elevated to the PI within 24 h*. We will suspend the participant's Text Buddy access immediately, and study staff will contact them by telephone to resolve the issue.

Methods for additional analyses

Secondary outcomes: (1) information about and (2) motivation for uptake of PrEP; (3) STI Testing; and (4) the impact of the intervention on mental health indicators. We will use generalized linear mixed models (with an identity link function) to test whether the intervention is associated with higher scores of PrEP information and PrEP motivation compared to the control. These models will utilize all seven time points, with time as an interaction effect to determine whether the score differences attenuate over time. Specific contrasts will be made to test for intervention effects at the end of the intervention and at 12 months post follow-up.

Given a focus of the intervention on reducing stigma, using substances during sexual episodes, and increasing social support to affect HIV preventive behavior and positive outcomes, we will examine whether those in the intervention have greater improvement on these mental health indicators over time than do those in the control. These models will be estimated in the same manner as PrEP information and motivation.

Unique statistical analysis challenges posed by an HIV incidence endpoint and approaches to manage other expected study outcomes

Because HIV incidence is a relatively rare event, it is challenging to have sufficient power to detect differences by experimental arms for this endpoint. This challenge is compounded by the fact that sero-positivity can sometimes take up to 3 months post-infection to detect. Nonetheless, even when we account for the possibility that we will miss youth whose HIV is not yet detectable, our observation period (from baseline to 12-month post-intervention follow-up) is 14 months. However, we submit that the study remains adequately powered to measure beyond 1-year incidence.

An incidence endpoint also requires that participants are sero-negative at baseline. This makes it challenging to recruit youth: A large number of youth who would otherwise take part if an HIV test result verification were not required will decline to assent/consent. We also will experience attrition between the consent/assent and randomization period because participants who are mailed the test do not take it, or they take it but choose not to upload the result in the baseline survey platform. To manage this, our plan assumes 25% attrition from assent/consent to randomization; we plan to assent/consent 6777 youth to randomize a sufficiently large sample, i.e., $n = 5000$.

Another challenge is how to treat youth who self-report HIV positivity but do not provide confirmation of the test. Those who provide photo-verification of a positive result are censored from subsequent data collection efforts. We will conduct sensitivity analyses to understand the implications of including these self-reported positive results as positive OraQuick-verified analyses versus treating them as negative.

Because of these noted challenges, it is even more important to manage other expected study outcomes in a way that increases the likelihood that true differences in experimental arms (i.e., intervention impact) are detected. To this end, we also will be analyzing self-reported HIV incidence; this will help address potential under-reporting by youth who do not want to upload their test result, especially a positive one. We also will analyze study endpoints that are expected to have higher prevalence and also be less stigmatizing to report the number of STIs, and uptake of PrEP and PEP. As proximal indicators of risk for HIV acquisition, these outcomes will further help contextualize the effect the intervention may have on HIV incidence.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data

Given that the program will be delivered via technology, protocol non-adherence could occur if there are technological challenges (e.g., systemic non-sending of text messages) or if participants purposefully misreport their PII to appear eligible when they are not. We will closely monitor software performance and quickly problem solve any technology issues to ensure that technology-related disruptions of message delivery do not affect the data. Any challenges will be noted by date and time in a "field blog" so that if systemic issues are noted, people affected by these issues can be examined separately in the

analyses to determine if their outcomes are different from unaffected youth. To reduce the likelihood of enrolling people who are ineligible, we will use logic in the screener to redirect ineligible people to a "thank you" page. We also will identify people with duplicate email addresses, phone numbers, and/or mailing addresses. Given the highly interactive nature of the program, we also will note interactions with participants that seem age incongruent (e.g., language used) and reach out to anyone flagged by research staff to further confirm their identity.

We will conduct sensitivity analyses to contextualize how assumptions about the missing data mechanism influence our understanding of intervention impact. To do so, we will follow recommendations made by Leacy et al. [57] and also analyze data with missing data coded as failure and with missing data coded as success.

Plans to give access to the full protocol, participant-level data, and statistical code

We provide full public access to the protocol through this document and upon request to clarify or offer more detail on specific study procedures. We will provide de-identified participant level data upon request when provided with a clear rationale and detailed analytic plan, e.g., for use in a meta-analysis. While our protocol includes details on analysis, we do not plan on releasing statistical code.

Oversight and monitoring

Composition of the coordinating center and trial steering committee

The research team will comprise the coordinating center. The team includes the PI, a project coordinator, research assistants, as well as multiple software developers and other technology support personnel. The team will meet weekly during the trial implementation to discuss recruitment, enrollment, intervention implementation, and documentation as well as any protocol deviations or adverse events should they arise. The trial steering committee comprises the PI, project coordinator, and 3 project co-investigators. This group will meet periodically to discuss project implementation.

Composition of the data monitoring committee, its role and reporting structure

The PI will be responsible for all aspects of the project with respect to intervention design, data collection, and use of data. Pearl IRB will approve all aspects of the study prior to commencing data collection. Informed youth assent or adult consent will be obtained from all participants. Participants will have access to referral information to resources that provide support 24 h a day (e.g., Trevor Project) as well as phone numbers for the study administrators (i.e., PI and IRB).

Data monitoring

Study staff will monitor the quality of the evaluation as it occurs, using our performance measure data. For example, we will monitor our adherence to the proposed timeline by tracking our enrollment rates, the percentage of youth who assent but do not complete the baseline survey (i.e., the baseline response rate), and our follow-up response rates. If response rates are lower than anticipated, the project team, including consultants, will convene and brainstorm ideas to invigorate survey completion. Intervention participation will be measured through the intervention's weekly level-up questions, the amount of interaction with their Text Buddy, the acquisition of badges, etc. Survey data will be monitored continuously to quickly identify any problems (e.g., programming of the skip patterns, unexpectedly high "do not want to answer" rates for questions).

We have developed, and will refine, an online monitoring interface for this project that allows project staff to monitor the program messages sent to participants, the messages that participants send to the program, and participants' progression through the program. Any problems with program functioning will be immediately elevated to the technology team to resolve.

Adverse event reporting and harms

We will promptly report unanticipated problems to the IRB and appropriate institutional officials of (i) any unanticipated problems involving risks to participants or others, or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval. The purpose of prompt reporting is to ensure that appropriate steps are taken in a timely manner to protect other participants from avoidable harm. To be specific, we will promptly report to the IRB:

- Deviations and violations in accordance with local, institutional, or protocol-specific guidelines/procedures
- Changes increasing the risk to subjects and/or significantly affecting the conduct of the trial
- Adverse events (definition per International Council for Harmonisation, Good Clinical Practice, and the Food and Drug Administration) as specified in the protocol or by IRB policy
- New information that may adversely affect the safety of the participants or the conduct of the study

In general, we will define "prompt" as, and report accordingly when possible:

- Unanticipated problems that are serious adverse events will be reported to the IRB within 1 week of the investigator becoming aware of the event
- Any other unanticipated problem should be reported to the IRB within 2 weeks of the investigator becoming aware of the problem
- All unanticipated problems should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and Office for Human Research Protections within 1 month of the IRB's receipt of the report of the problem from the investigator

The PI will review the project progress and the collected data to ensure that potential adverse effects, if they occur, are identified and reported to the IRB. Any action recommended by the IRB will be implemented immediately in order to minimize further risk. All notifications will be done via email.

Frequency and plans for auditing trial conduct

We have a data safety and monitoring plan as described above re: interim analyses. Our team will review progress on achieving enrollment goals each week and will monitor intervention delivery to document and address any technology errors or failures on a daily basis during study implementation.

Plans for communicating important protocol amendments to relevant parties (e.g., trial participants, ethical committees)

We do not anticipate any changes to eligibility criteria, outcomes or analytic plans that are described here. However, if any of these do occur, we will submit amendments to our IRB for review and approval and will make modifications to our ClinicalTrials.gov registration, if necessary. Such amendments are not communicated to participants unless it would affect their own eligibility and continued enrollment in the trial.

Dissemination plans

We have a multi-tiered dissemination plan. For researchers, we will publish our findings widely in peer-reviewed journals. We also will present findings at at least two professional conferences (e.g., AIDS). We will not utilize professional writers, and authorship eligibility guidelines will conform to guidelines published by Fontanarosa et al., in 2017 [63]. For both researchers and public consumers, we will create a webpage on the CiPHR website where people will be able to download all study materials, journal, articles, and media mentions about the study free of charge. Finally, we will register with ClinicalTrials.gov.

Discussion

Although this proposal is highly significant and innovative, it is not without limitations: (1) While 12 months is a sufficient follow-up period, 24 months would have been preferred. We chose to preference sufficient time for recruitment and enrollment to ensure a sufficient sample size over a longer follow-up period with a smaller sample. We also deemed it unlikely that differences in incidence, which is a low occurring event, would be detectable through 24 months without ongoing intervention into the second year. (2) It bears noting that the OraQuick home-based HIV test may not detect infection that has occurred within the past 3 months. If we "adjust" our surveillance period for this possibility, we will still be measuring prevalence across 14 months from baseline to 12-month follow-up. (3) It also would be preferred to confirm HIV sero-status using blood assays. Based upon the conversations we had with colleagues, however, we believe the impact this type of test would have on our response rate would make it impossible to reach our recruitment and retention goals. (4) Additionally, it would potentially be transformative if we could mail PrEP to our participants. That said, even if we could identify a way to remotely prescribe to participants—including those under 18 years of age, the sustainability of such a program after the study ends is highly questionable, and the benefit of technology-based interventions is their low cost and scalability. It also may bear noting that an intervention centered on the mass distribution of PrEP is less about behavioral interventions that impact HIV incidence and more about whether people will uptake PrEP if it is proactively mailed to them. The data are very clear on PrEP's preventive impact. Understanding the impact that increased access would have on incidence is an important research question, but one the current study. (5) Some also may have concerns about the feasibility and acceptability of such an intense, long intervention. Our previous work suggests reason for optimism. (6) It also bears noting that not all youth will have unlimited Internet bandwidth, reducing their access to videos. The intervention text messaging content is written to stand alone however, so we believe that this will not be a significant limitation. (7) Finally, gender diverse youth are excluded. This is because the time necessary to develop content that is appropriately gender affirming is more than what is afforded in the first year of the grant.

The rigor of the proposed study is high: Random assignment eliminates the possibility of youth being purposefully assigned to a particular study arm. The

attention-matched control will reduce the likelihood that behavior change, if detected, is due to the "attention" youth received by the daily messages. Moreover, the population-based focus on the intervention design and pilot testing increases the generalizability of findings beyond cisgender sexual minority boys and young men living in one city or a particular region, and increases the likelihood that the program could feasibly be disseminated at the public health level. The manner in which youth are recruited will increase the likelihood that the sample reflects youth who might use the intervention if it were available publicly (e.g., the lack of incentives for the baseline survey, the lack of mention of incentives in recruitment ads), while also increasing the likelihood that they are who they say they are (e.g., telephone enrollment).

In conclusion, because of our population-based approach to finalizing and testing the intervention, if findings are positive, the intervention can be quickly made publicly available to affect HIV incidence at the population level.

Trial status

Protocol date: 5/31/2023. Date recruitment began: January 15, 2024. Approximate date recruitment will be completed: January 15, 2027.

Appendix

PROJECT SHAG RCT CONSENT FORM

STUDY TITLE: HARNESSING THE POWER OF TEXT MESSAGING TO REDUCE HIV INCIDENCE IN ADOLESCENT MALES ACROSS THE UNITED STATES

FUNDER: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT GRANT NUMBER: U01HD108738

SPONSER: CENTER FOR INNOVATIVE PUBLIC HEALTH RESEARCH (CIPHR) PRIMARY INVESTIGATOR: MICHELE YBARRA, MPH PHD

The Center for Innovative Public Health Research has developed two sexual health programs for guys who are into guys. You are being asked to take part in the randomized controlled trial of the two programs to see which one works better. The programs will be sent through text messaging. Program text messages talk about things like safely having sex with guys, ways to prevent HIV and other STIs, and using condoms and PrEP.

This research study is sponsored by the National Institutes of Child Health and Human Services.

Procedures

Your participation will last about 18 months.

You are one of about 5,000 guys 13–22 years old being invited to take part in the Project SHAG study. SHAG stands for: Sexual Health Advocacy for Guys.

There are two different text messaging programs that we are testing. We do not know which program is better at promoting healthy sexual behavior. You will be randomly assigned to either program. This means you have an equal chance of being in either program. We will not tell you which program you are assigned to until after everyone has finished the program.

If you choose to take part in the research study, here's what we will ask you to do:

1. Complete an online survey and an HIV test before you start the program. We will mail you the test. You can do it anywhere and anytime that is safe for you. We ask you to upload a picture of the results of the test to our secure study server so that we are on the same page about your result. Only the research team will have access to the picture; we take your privacy seriously.
2. Once you finish the survey and upload your test results, you will be officially enrolled. You will receive between 5–10 text messages every day for 9 weeks. You may also be randomly matched to a "text buddy", another guy in this study, who you will be able to talk to about the things that you are learning in the program.
3. After 9 weeks, the daily text messages will stop, and we will ask you to complete another online survey.
4. We will then send you a couple of texts per week for the next 3 months.
5. After that, you will receive a "review week" where you will receive 5–10 messages again each day. After the review week, we will send you another HIV test and a survey link and ask you to upload your test results and do the online survey.
6. Over the next 12 months, we will ask you to do 4 more online surveys, once every 3 months. At 12 months, as part of your last survey, we will send you a final HIV test and ask you to upload a picture of the results to the secure Project SHAG server.

The only cost for you to take part in this study will be costs that you already pay for text messaging and to go online. We will pay for the HIV tests and the shipping costs.

Incentives

You can receive up to $270 for taking part in this study. Here's how it breaks down:

For doing the online surveys, you'll get:

- $15 for completing the 'core' intervention end survey at 9 weeks
- $15 for completing the intervention end survey at 5.5 months
- $25 for completing the 3-month survey after the end of the intervention
- $25 for completing the 6-month survey after the end of the intervention
- $25 for completing the 9-month survey after the end of the intervention
- $30 for completing the 12-month survey after the end of the intervention

You can also earn a bonus if you upload your HIV test:

- You can earn a $30 bonus for uploading your fist test result in the first survey
- You can earn a $45 bonus for uploading your second test result at the end of the intervention, 5.5 months later
- You can earn a $60 bonus for uploading your third test result at the end of the study

You may choose not to upload a photo of your results. In this case, you will not get the bonus. It is also possible a different bonus may be offered during your time in the study.

Your incentives and bonuses will be sent to you as an Amazon gift card to the email address you give us. You will also have the option to donate your incentive to a charity, or choose not to get an incentive at all. You may be asked to confirm your identity by verifying your personal information at any time during the study. You can do so by joining a video call with study staff or sending us a copy of your government issued ID, among other methods. Not confirming your identity may result in being removed from the study and not getting paid your incentives.

Risks and Discomforts

It is possible that you will learn that you have HIV. This could be very upsetting. Some guys experience problems with family or have emotional difficulty learning that they are HIV positive. If you are worried about whether you can stay safe if you learn you have HIV, this might not be the right time for you to be in this study.

It is also possible that your privacy will be broken. For example, someone might see the shipping package, the HIV test, the program text messages or the online survey on your device and ask you about it. We want to protect your privacy as much as possible so it is very important that you have the HIV test mailed somewhere that is safe for you, and that you take the test in a private place.

It also is important that you receive the program text messages and take the surveys on your own private device – not one you share with others. If your phone is linked to another device like a family-shared tablet, maybe think about being sure that the messages don't scroll on this other device.

Survey questions we ask might make you feel uncomfortable. If this happens, you can select 'Do not want to answer;' leave the survey and not answer the question; or stop being in the study completely. Please know that some questions, such as your birthday, are required if you want to take part.

It also is possible that something else might happen that we have not thought about yet.

Benefits

You may benefit by knowing your HIV status. If you are positive, you can start lifesaving treatments. If you are negative, you can continue making choices to reduce your risk of getting HIV, like using condoms or getting on PrEP (a pill or shot that reduces your chance of getting HIV). You may also learn ways to have a healthy sex life.

Rights of Refusal and Withdrawal.

You can choose to be in the study or not. If you decide not to be in the study, that is OK; nothing bad will happen.

You can choose to stop being in the study at any time, even if you have already started. If you decide you do not want to be in the study after it has started, just let us know by texting us at 714- 203–2755.

Your time in the study may also stop at any time for any reason, such as, the sponsor or the study investigator decides to stop the study.

Confidentiality

We will keep a copy of your answers after the study ends so that we can look at them later. We will only share research data where we have removed anything that we think would show your identity. There still may be a small chance that someone could figure out that the information is about you. Examples of sharing include:

- Publishing results in a book or journal.
- Adding results to a federal government database.
- Using research data in future studies, done by us or by other scientists.
- Representatives at the Department of Health and Human Services and Pearl IRB also may request access to the study data.

We will analyze your responses to the surveys and the messages to determine which program is better. If you

are matched with a Text Buddy, we may also analyze your conversation to better understand the lives of guys today and also identify ways to improve Project SHAG. We may also use study data to look at another research question that we have not thought of yet.

Aside from the sharing of research data we note above, we will not tell anyone what your HIV test result is, or what your answers are on the surveys.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. This Certificate means that we can keep your information private even if we get a court order telling us to share your information. We will use this Certificate to fight demands for your information unless you tell us you want us to share the information. In the unlikely event that you tell us that you are being harmed or harming others, then under applicable law, we may be required to report this information to the appropriate authorities.

Questions and Contact Numbers

The researchers do not have a conflict of interest in this study.

If you have questions about the study or any concerns about the study questions, please contact:

- Dr. Michele Ybarra toll-free at 1–877-302–6858 ext. 801 or Michele@InnovativePublicHealth.org.
- If you have questions about your rights as a participant in this study, or if you feel that you have been harmed in any way by taking part in this study, please contact Pearl IRB:
    - By mail: Study Subject Adviser Pearl IRB 29 East McCarty Street, Suite 100 Indianapolis, IN 46225 or
    - Call: 317–899-9341 or
    - By email: info@pearlirb.com

An IRB is a group of people who review research studies to protect the rights and safety of research participants. Please reference the following study title when contacting the Study Subject Adviser: Project SHAG.

Here are some resources that you may find helpful:

- If you would like to find a clinic where you can get tested for HIV, go here: https://gettested.cdc.gov/
- Here is information about HIV: https://www.cdc.gov/hiv/basics/whatishiv.html, and resources for people who are living with HIV: https://www.cdc.gov/hiv/basics/livingwithhiv/resources.html
- You can always talk to someone at the Trevor-Project for support. They have a 24-h hotline for LGBT + youth: 1–866-488–7386, or text 'START' to 678678.
- If, at any time, you think about hurting yourself, please contact the National Suicide Prevention Hotline at: 988. They can help.

Do you want to take part in this 2-year study? No.

Yes.

[If the person agrees to take part in the study:]

Can we contact you after the study ends if we have questions for you about the study? No.

Yes.

[Asked of everyone].

Would you like us to tell you about other studies that you might be eligible for? No.

Yes.

[If the person declines to take part in the study:]

We respect your decision. So that we can better design studies in the future, could you please share why you would not like to be part of Project SHAG?

[non-mandatory text box].

Abbreviations

CiPHR	Center for Innovative Public Health Research
FB	Facebook
FDA	Food and Drug Administration
G2G	Guy2Guy
HIV	Human immunodeficiency virus
IG	Instagram
IRB	Institutional Review Board
MTL	Molecular Testing Labs
PEP	Post-exposure prophylaxis
PI	Principal Investigator
PII	Personal Identifying Information
PrEP	Pre-exposure prophylaxis
RCT	Randomized controlled trial
SGM	Sexual and gender minority
SHAG	Sexual Health Advocacy for Guys
SPIRIT	Standard Protocol Items: Recommendations for Intervention Trials
STI	Sexually transmitted infections

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

MY is the Principal Investigator; she conceived the study, led the proposal and protocol development. RG and SB contributed to study design and to development of the proposal. DF was the lead trial methodologist. All authors read and approved the final manuscript.

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Data availability
We will make limited datasets available to researchers with detailed proposal, IRB supervision and the appropriate data use agreements in place.

Declarations

Ethics approval and consent to participate
Pearl IRB reviewed and approved the study protocol. The reference number is 21-CIPH-106. Oral informed consent for those 18 years of age and above, and assent for those under 18, will be obtained from all participants. A waiver of parental permission for those under 18 years of age has been approved by the IRB.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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