Title: A Pragmatic Trial of Two Strategies for Implementing an Effective eHealth HIV Prevention Program (Keep It Up! 3.0)

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A pragmatic trial of two strategies for implementing an effective eHealth HIV prevention program (Keep It Up! 3.0)

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Summary of IRB Submissions, Modifications, Continuing Reviews

IRB ID# (STU) Mod#/CR#	Type of Submission	Date of Approval	Description - Summary of changes
STU00207476	Initial, JIT	08 May 2018	Just-in-Time Pre-Approval of NIH protocol
MOD001 (12 May 2018)	Mod to other parts of the study (Phase 1)	18 May 2018	Seeking IRB approval for NIH award process; Phase 1 documents (recruit script, consent, interview questions) for Usability Testing
MOD0002 (23 Oct. 2018)	Minor update to study team member information	23 Oct. 2018	Adding study team member as authorized research personnel
MOD0003 (8 Jan. 2019)	Mod to other parts of the study	28 Jan. 2019	Seeking IRB approval for considering our community based partner sites as not engaged in research
MOD0004 (1 Feb. 2019)	Minor update to study team member information	1 Feb. 2019	Adding study team member as authorized research personnel
MOD0005 (8 Feb. 2019)	Minor update to study team member information	8 Feb. 2019	Adding study team member as authorized research personnel
CR0001 (27 March 2019)	Continuing Review	25 April 2019	Continuing Review
MOD0006 (22 Feb. 2019)	Minor update to study team member information	6 June 2019	Adding study team member as authorized research personnel
MOD0007 (10 May 2019)	Mod to other parts of the study	24 May 2019	Updating protocol to include description of online training courses for CBO partner sites
MOD0008 (8 Aug. 2019)	Mod to other parts of the study	19 Aug. 2019	Updating to include info on DTC recruitment strategies, eligibility screening, consent process, and compensation.
MOD0009 (5 Sept. 2019)	Mod to other parts of the study	11 Sept. 2019	Updating study measures
MOD0011 (27 Sept. 2019)	Minor update to study team member information	27 Sept. 2019	Adding study team member as authorized research personnel
MOD0012 (15 Oct. 2019)	Minor update to study team member information	15 Oct. 2019	Adding study team member as authorized research personnel
MOD0013 (25 Oct. 2019)	Mod to other parts of the study	20 Nov. 2019	Updating medical record release authorization with more precise language and new timeline
MOD0014 (7 Jan. 2020)	Mod to other parts of the study	13 Jan. 2020	Updating protocol to clarify that CBO partner sites have the option to provide clients with their local medical record release authorization form
MOD0015 (10 Feb. 2020)	Minor update to study team member information	10 Feb. 2020	Adding study team member as authorized research personnel
MOD0016 (6 Mar. 2020)	Mod to other parts of the study	18 Mar. 2020	Updating protocol to allow participants in DTC arm to enroll without self-reported HIV

			negative or unknown status, replace the eligibility screener with a registration form in DTC arm, and increase raffle amount for $50 to $200.
MOD0017 (8 April 2020)	Mod to other parts of the study	24 April 2020	Updating CBO arm consent form to clarify when participants are entered into raffles for a gift card.
MOD0018 (22 May 2020)	Mod to other parts of the study	9 July 2020	Updating protocol to allow participants to complete at-home HIV testing with blood spot test kit, participant incentives of $10 and $25 for completing first three sessions of intervention, and updating consent forms with new incentive information.
MOD0019 (12 June 2020)	Minor update to study team member information	12 June 2020	Adding study team member as authorized research personnel
MOD0020 (14 July 2020)	Mod to other parts of the study	14 August 2020	Updating consent forms with payment information in “Key Information” section and adding consent form for participants who are ineligible for research component of the study but allowed to access service project component (i.e. intervention content).
MOD0021 (12 August 2020)	Minor update to study team member information	12 August 2020	Adding study team member as authorized research personnel
MOD0022 (14 August 2020)	Mod to other parts of the study	16 September 2020	Updating protocol to reflect a new recruitment collaboration with Trialfacts and change to our eligibility criteria to allow male assigned at birth participants who identify as gender non-conforming. RSS data security form also updated with info about video conferencing software used for qualitative interviews.
MOD0023 (10 Dec 2020)	Minor update to study team member information	10 December 2020	Adding study team member as authorized research personnel
MOD0024 (22 January 2021)	Mod to other parts of the study	19 February 2021	Updating protocol and consent forms to reflect changes to study design and aims, eligibility criteria, and intervention schedule. New qualitative interview guide and surveys for CBO partner sites, updated online ad samples for the DTC arm, new medical record release form for DTC arm, email templates for alerting participants to changes, and materials from DSMB are also submitted.
MOD0025 (5 February 2021)	Minor update to study team member information	5 February 2021	Adding study team member as authorized research personnel
MOD0026 (24 February 2021)	Mod to other parts of the study	8 March 2021	Updating protocol and CBO registration form, and administering new questions to CBO participants as means of assessing if STI testing was done on site at CBOs and if CBO participants would like to be shipped at-home STI test kits by the KIU! team. Also updating the CBO staff survey and interview guide.
MOD0027 (29 March 2021)	Mod to other parts of the study	28 April 2021	Updating protocol and consent forms to reflect new $10 incentive for participants who complete optional self-administered, at-home STI testing at 12-week follow-up
MOD0028	Mod to other parts of	8 June 2021	Updating the DTC arm consent form to remove

	the study		Visa branding from the incentives given post-intervention and at 6 and 12 week follow-up. Also removed two study team members and added one study team member as authorized research study personnel.
MOD0029	Minor update to study team member information	16 June 2021	Adding study team member as authorized research personnel.
MOD0030	Minor update to study team member information	7 July 2021	Adding study team member as authorized research personnel.
MOD0031	Minor update to study team member information	9 July 2021	Adding study team member as authorized research personnel.
MOD0032	Minor update to study team member information	29 July 2021	Adding study team member as authorized research personnel.
MOD0033	Minor update to study team member information	26 August 2021	Adding study team member as authorized research personnel.
MOD0034	Minor update to study team member information	1 September 2021	Adding study team member as authorized research personnel.
MOD0035	Mod to other parts of the study	Pending	Updating protocol to reflect new strategies for confirming identities of participants enrolled in the DTC arm of the study.
MOD0036	Minor update to study team member information	10 September 2021	Adding study team member as authorized research personnel.
MOD0037	Minor update to study team member information	27 September 2021	Adding study team member as authorized research personnel.
MOD0038	Mod to other parts of the study	21 December 2021	Updating CBO arm consent form to state that participants will have the option to receive an Amazon or Visa e-gift card for completing 12-week STI testing.
MOD0039	Minor update to study team member information	14 December 2021	Adding study team member as authorized research personnel.
MOD0040	Minor update to study team member information	13 January 2022	Adding study team member as authorized research personnel.
MOD0041	Minor update to study team member information	18 January 2022	Adding study team member as authorized research personnel.
MOD0042	Minor update to study team member information	3 March 2022	Adding study team member as authorized research personnel.
MOD0043	Minor update to study team member information	10 June 2022	Adding study team member as authorized research personnel.
MOD0044	Minor update to study team member information	28 June 2022	Adding study team member as authorized research personnel.
MOD0045	Minor update to study team member information	6 July 2022	Adding study team member as authorized research personnel.
MOD0046	Mod to other parts of the study	17 August 2022	Updating protocol and consent forms to reflect new $20 incentive for completing 12 week-

			follow-up survey and $20 for completing at-home STI testing at 12-week follow-up
MOD0047	Mod to other parts of the study	Pending	Updating protocol to reflect DTC staff will complete a short survey and qualitative interview.

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PHASE 1	**Project Year 1**	**Hiring, KIU Content Revisions, Usability/Acceptability Testing**
Phase 1a	**(0-6 month)**	Hiring and KIU Content Production and Adaptation for Delivery, Updating Technology and Refreshing Content, Develop/Release/Promote RFAs
Phase 1b	**(6-12 months)**	Advisory Board/Consultant Meetings,Qualitiative Interviews with CBOs Usability Testing, Recruitment Materials for CBO Arm, select CBOs from counties randomized to CBO Arm, Creating Recruitment Plan for DTC Arm, Selecting Measures, Developing HIV/STI testing protocols for both Arms, Finalizing Consents (online and in person) for KIU! enrollement for both Arms
Phase 2	**Project Years 2-4**	**Begin Recruitment and Launch KIU! Implementation Trial**
		Final CBO selection/subcontracts/training/launch with tech support Final DTC recruitment and launch of KIU! for enrolled subjects
Phase 3	**Project Years 4-5**	**Assess Implementation, Effectiveness, and Cost Analyses**
		Qualitative Interviews with CBOs, cost and effectiveness data collection for implementation measures/strategies, creating and delivery sustainability plan with CBOs, data cleaning/analysis and dissemination plan

SPECIFIC AIMS

Substantial effort has gone into developing and testing the efficacy of eHealth HIV prevention interventions[1-5], but these interventions will not affect the spread of the epidemic unless they are implemented effectively to reach the most at-risk populations. Despite emerging evidence that eHealth approaches can be highly effective in reducing HIV risk or improving care engagement[5-8], their implementation requirements do not fit within established strategies for public health scale up,[9, 10] leaving it an open question as to how to bring these programs into practice. To date, little to no implementation science has examined strategies to effectively scale up eHealth HIV prevention programs.[9, 10] The overarching goal of this proposal is to address this need by developing and evaluating novel strategies for implementing eHealth HIV prevention programs. Keep It Up! (KIU!) is an online program proven to reduce HIV risk among diverse young men who have sex with men (YMSM).[11-14] KIU! was designed for YMSM who just tested HIV negative to *keep it up* and maintain their negative status by reducing risk and enacting protections. Strong evidence of effectiveness on behavioral (decreased condomless sex) and biomedical outcomes (reduced STI incidence) makes KIU! an ideal eHealth intervention for implementation research. Lessons learned from KIU! implementation will set the pathway for implementing the many HIV eHealth programs currently undergoing efficacy testing.

Implementation strategies need to be evaluated using rigorous research designs.[15] Through formative research with community-based organizations (CBOs), health departments, the CDC, and researchers we have identified two pragmatic implementation strategies that we will evaluate and compare: In Strategy 1, CBOs apply for, and are selected for, funding to deliver KIU! through their current HIV testing programs. Because CBOs do not have the capacity to host the technology, KIU! is hosted centrally at Northwestern and deployed by local CBO staff. Training and coaching of CBO staff on how to use the technology and integrate it into routine HIV testing is provided through capacity building assistance. Strategy 2 is a "direct-to-consumer" (DTC) model where centralized staff at Northwestern recruit participants nationally through online advertising campaigns and manage their engagement. HIV/STI testing kits are shipped directly to YMSM, and upon documentation of an HIV negative test result, participants are delivered KIU! This DTC model has been widely adopted in technology dissemination,[8, 17, 18] but it is innovative in terms of implementation of HIV prevention programs.

We will accomplish our goal to inform eHealth intervention implementation with 2 specific aims:

Aim 1: Compare two implementation strategies using a quasi-experimental trial. We selected a type III hybrid implementation-effectiveness design[19], which prioritizes empirical comparison of implementation strategies while also collecting evidence of effectiveness. KIU! will be delivered using Strategy 1 (CBOs) in 22 counties for two years; simultaneously, we will delivery KIU nationally using Strategy 2 (DTC). YMSM participants in the DTC strategy will be matched to CBO strategy participants based on post-hoc propensity scores. Implementation and effectiveness outcome data collected from YMSM participants, CBOs, and the technology vendor. Our primary outcomes are public health impact (defined as reach X effectiveness[20-22]) and cost per infection averted, a key component of CDC decision making about which HIV prevention programs will be supported.[23, 24] There continues to be equipoise for the trial (i.e., either strategy could be superior). Because implementation success can be defined differently for different stakeholders[25], we will also collect and report as secondary outcomes multiple metrics of reach, effectiveness, and implementation.[21]

Aim 2: Examine adoption characteristics that explain variability in implementation outcomes. There is remarkable variability in implementation success when CBOs adopt evidence-based interventions.[26-28] We will seek to explain variability in implementation success across counties by conducting mixed-methods research[29, 30] on the domains from the consolidated framework for implementation research (CFIR)[31], such as county characteristics, adaptations, support from organization leadership, and approach to planning adoption. Data on CFIR characteristics will be collected through administrative data, surveys, and telephone interviews with key stakeholders.

In addition to our 2 specific aims, we will **explore sustainment of KIU! at the completion of the study.** CBOs will be provided with materials to facilitate applying for external funding to continue to provide KIU! after study

completion, including an Impact Tool[32] to estimate local impact and costs. We will also examine factors that predict applying for funding and ongoing sustainment.[33] For Strategy 2, through consultation with the CDC, capacity building assistance providers, health departments, and small businesses involved in Health 2.0 initiatives, we will examine models for ongoing sustainment of the DTC model.

This application is in response to PA-17-194 that calls for targeted implementation science for HIV prevention and treatment, including studies to optimize implementation of behavioral risk reduction interventions. It is consistent with the NIH Office of AIDS Research's high priority of implementation science to improve entry into prevention services and reduce disparities in new infections.

A. SIGNIFICANCE

A.1. The burdens of HIV and STIs fall disproportionately on YMSM. YMSM (aged 18–29) account for nearly 70% of all new HIV diagnoses among adolescents and young adults in the U.S.[34], with HIV prevalence estimated at 13.5% in 18–24 year-olds and 17.8% in 25–29 year-olds. Black YMSM experience the highest prevalence (36.0%).[35] The CDC estimates that since 2010, the diagnosis rate has increased 18% among Latino YMSM,[36] which is consistent with our simulation model of future HIV incidence among YMSM.[37] HIV infections among YMSM are almost entirely transmitted via unprotected sex,[38-41] defined here as sex with neither PrEP nor condoms. STI prevalence is also high among YMSM,[42-44] and STIs play an important role in increasing HIV transmission.[45-47] In fact, the CDC estimates a rectal STI causes a threefold increase in the per-act risk of HIV transmission during receptive anal sex.[48] In the *Keep It Up!* (KIU!) 2.0 trial of 901 YMSM, we found 13% tested positive for rectal Gonorrhea or Chlamydia at enrollment.[49]

A.2. As alarming as these epidemiological data are, there has not been a commensurate prevention response. While research attention has increased on YMSM, our recent analysis of the CDC's *Compendium of Evidence-Based HIV Prevention Programs*[50] found that only 2 out of 93 programs focused on YMSM (i.e., Mpowerment and Young Men's Health Project).[51] Programs designed more broadly for all adult MSM do not tend to effectively engage YMSM; for example, a recent study in Los Angeles found that the average age of MSM who participated in HIV prevention programs was 40–49 years old.[52] This likely reflects the reality that **YMSM have unique prevention needs[53]** and that programs designed for older adult MSM may not generalize to the developmental context of emerging adulthood—the unique period during which individuals are "too old" to be adolescents (>18) but not "old enough" to be adults (~29).[54, 55]

A.3. The impact of available HIV prevention evidence-based interventions (EBIs) has been insufficient to meet goals for reducing HIV incidence. The current arsenal of behavioral EBIs primarily includes face-to-face individual and small-group programs[50], and their reach has been limited by economic and structural barriers to implementation.[26, 27, 56-59] Only 28% of HIV negative urban YMSM report participating in an HIV prevention program.[35] EBIs have typically been delivered through practice settings such as health departments and CBOs,[60-62] and evidence suggests interventions are not always implemented with fidelity,[26-28] which can produce a "voltage drop" in effectiveness.[63] Recently, the Director of the CDC Division of HIV Prevention stated, "Effective implementation is our greatest challenge."[64] The NIH Office of AIDS Research includes implementation science to improve entry into prevention services as a high priority topic.[65]

A.4. eHealth represents an opportunity to deliver effective interventions to large numbers of diverse YMSM. Digital technologies, collectively termed "eHealth", are becoming increasingly more integrated into healthcare and public health practice.[66] With >92% of young adults across all races and income levels going online daily, particularly via smartphones,[67] eHealth approaches represent a critical modality for engaging YMSM and delivering intervention content directly to "where they are" while overcoming barriers to access (e.g., geography[68, 69]) and circumventing delivery challenges (e.g., fidelity[51]). Evidence from systematic reviews and meta-analyses indicate that eHealth programs have significant effects on HIV risk and protective behaviors comparable to in-person EBIs.[6, 8, 70, 71] Additionally, eHealth has been shown to improve youth access to healthcare services[72] and rates of HIV testing.[73] The potential for cost-efficient scalability and flexible dissemination is a major boon for eHealth HIV prevention among YMSM.[8, 71, 74-76]

A.5. The KIU! online intervention capitalizes on HIV testing as an opportunity to increase reach and reduce risk. This innovative approach linking an eHealth intervention to testing serves two goals:

(1) Efficient reach to diverse YMSM. Most urban YMSM have recently been HIV tested (76% in prior 12 months), with little difference by race/ethnicity.[35] HIV testing comprises a large proportion of the CDC's prevention budget;[77] therefore, linking to testing increases the potential for sustained intervention reach and integration into standard care. Importantly, linking an eHealth intervention to HIV testing is a proven engagement strategy for racial/ethnic minority YMSM who are at increased risk.[78]

(2) Fulfilling an unmet need for greater prevention in the context of testing. Research is mixed on the effectiveness of standard counseling and testing in reducing risk behaviors among those who test

negative.[79, 80] In the absence of an intervention, repeat negative test results are correlated with increased HIV risk behaviors in MSM,[81] perhaps because of perceived invulnerability after multiple negative results.[82, 83] There is also evidence that prevention counseling is not routinely provided across settings[84] and is highly variable in quality.[79] As such, a proven-effective behavioral intervention, linked to HIV testing and delivered with fidelity, would be highly impactful. Furthermore, linkage from HIV testing to other prevention services has been shown to be a challenge due to service fragmentation, lack of support systems for linking and tracking, and lack of capacity of organizations that conduct testing to deliver YMSM specific interventions.[85] This is a missed opportunity for prevention with high-risk YMSM. Our goal is to make testing an opportunity for health promotion by "capturing" YMSM in a "teachable moment" via technology that is accessible, engaging, and behavior changing.

A.6. Our strong scientific premise is based on evidence that the theory-based KIU! is effective at reducing HIV risk in diverse YMSM and that our design is grounded in established implementation science models. KIU! was developed based on the Information-Motivation-Behavioral Skills model of HIV risk behavior change,[86, 87] which has been applied to YMSM,[88] and relapse prevention[89], which focuses on identifying triggers for risk and using cognitive-behavioral strategies to break the link from triggers to risk.[90, 91] KIU! was found to significantly reduce condomless anal sex in a pilot RCT[12] and to significantly reduce rectal STIs in a large effectiveness RCT[14] (see C3). When implemented as a prevention service by a CBO, an evaluation of KIU! demonstrated significant effects with no evidence of "voltage drop."[11] KIU! is one of the first eHealth HIV interventions with this level of evidence, and as such, it is the ideal intervention to study how to scale up. With many other HIV eHealth interventions currently being supported by NIH for development and testing of effectiveness, now is a critically important time to study how to implement these interventions.[2, 3, 70]

KIU! is also highly relevant in an era of multiple prevention options. We hypothesize that KIU! can increase PrEP uptake using the same core behavioral change principles that were effective in decreasing condomless sex and STIs (see C3). However, because PrEP received FDA approval after the launch of our recently completed RCT, it remains critical to investigate KIU's effectiveness in improving PrEP uptake among YMSM. Furthermore, not all MSM will use PrEP—particularly emerging adults, based on published levels of interest and uptake[92-94]—so condoms and STI testing and treatment will continue to be critical strategies for preventing HIV infections in this population.

The RE-AIM model[22, 95] has been widely used in implementation science[95, 96] and applied to eHealth[97, 98] and HIV prevention.[99] This model emphasizes dimensions of Reach, Effectiveness, Adoption, Implementation, and Maintenance. Consistent with recommendations to use mixed-methods approaches when assessing RE-AIM constructs,[95] the current proposal collects quantitative data on Reach, Effectiveness, and Implementation in Aim 1, mixed-methods data on Adoption in Aim 2, and qualitative data to explore Maintenance/Sustainability. Our use of the RE-AIM model is supplemented by implementation science frameworks used to identify organizational characteristics related to implementation success[31] and to predict sustainment.[33, 100] As such, our proposal's strong scientific premise is supported through existing evidence of program effectiveness and our utilization of health behavior change and implementation science theories.

B. INNOVATION

This proposal to inform the implementation of eHealth HIV prevention interventions is highly innovative for many reasons:

(1) The content of the KIU! online intervention. We created an online intervention that is highly interactive, engaging, and culturally-relevant (see Appendix 1). KIU! uses an innovative approach that focuses on situations and settings commonly experienced by YMSM (e.g., dating, meeting guys on apps). Intervention content is mapped onto these settings. This is different from traditional HIV prevention programs, which often have each session focused on an aspect of HIV knowledge, transmission, or prevention. KIU! makes extensive use of video, games, animation, and humor (when appropriate) to help increase engagement and motivate behavior change.

(2) At-home HIV and STI testing. A novel method of mitigating barriers to regular HIV testing[101-105] is to facilitate HIV self-testing through a DTC model. HIV self-testing has been demonstrated to be accurate, acceptable, and feasible, especially among those who may not otherwise seek an HIV test.[106-112] A recent systematic review by WHO found that HIV self-testing nearly doubled uptake of testing among MSM, compared to traditional testing methods, and found no indication of harm related to self-testing.[113] An even higher rate of screening was found among those who self-tested for STIs, with one meta-analysis reporting an 11-fold increase in testing compared to those who tested in a clinic setting.[114] While each of these meta-analyses strongly advocate for self-testing of HIV and STIs, neither were conducted specifically on YMSM. Our own recently completed RCT of KIU! (see C3) found the HIV/STI home testing approach to be highly acceptable and effective, suggesting it merits further investigations as a strategy for increasing rates of HIV/STI testing among YMSM.

(3) Our focus on eHealth implementation science. Effective implementation has been described as the greatest challenge to HIV prevention,[64] yet there has been insufficient research testing implementation strategies that will ensure effective interventions get to the right individuals at the right time in the right dose.[26, 59, 115] While prior implementation science has compared capacity-building approaches for individual and small-group prevention programs,[28, 58, 116, 117] there has been little-to-none on eHealth HIV prevention.[3, 8, 70, 71] The proposed study will lead the way in understanding the implementation of eHealth HIV prevention interventions to ensure the promise of cost-effective scalability is realized.[118]

(4) A large cluster randomized trial (CRT) is innovative in HIV research. CRTs are RCTs in which the units of assignment are groups or clusters. Methods for these trials are well developed.[119-121] There has been a recent increase in their use in public health and medicine,[119] but with a few important exceptions (e.g., HPTN 071 PopART[122] testing combination prevention in Africa; HPTN 043 Project Accept on community-based HIV testing in Africa and Thailand[123], and others[124, 125]), they have not seen significant application in HIV implementation science, particularly domestically. Our design of systematically selecting counties with large YMSM populations and then randomizing them to an implementation strategy is innovative. Particularly innovative is our plan to conduct a request for proposals from CBOs in eligible counties. This approach is pragmatic in that it matches the approach used by the CDC and health departments to distribute prevention funds to CBOs.

(5) Comparing DTC delivery versus CBOs implementation strategies. Both are viable strategies for eHealth intervention dissemination: The DTC model is a widely used technology dissemination approach[8, 17, 18] and is feasible to implement through a national coordinating center (such as a CDC-funded capacity building provider); The CBO model, with CBOs directly funded by the CDC or their local health department,[77] is the current backbone of implementing HIV prevention programs. While these are two viable implementation strategies, their relative advantages and disadvantages are unknown, and we do not know the circumstances where one is more valuable than the other. By evaluating both strategies head-to-head in this large trial, we will be able to discern their overall effectiveness and identify key moderating factors[31, 126] that could help boost and shape future dissemination and implementation of eHealth HIV prevention interventions[127, 128] and contribute to greater scalability, reach, and public health impact.

C. APPROACH

C.1. Investigative Team. The interdisciplinary investigative team has complementary expertise in eHealth research, implementation science, working with CBOs, distance testing for HIV and STIs, economic evaluation of healthcare innovations, recruitment and retention of diverse YMSM, and quantitative and mixed methods. This proposal benefits greatly from the **resources of the centers collaborating on this proposal**, including those at Northwestern (e.g., Center for Prevention Implementation Methodology [Ce-PIM], Center for Behavioral Intervention Technologies [CBITs]), the multi-institutional Center for Health Economics of Treatment Interventions for Substance Use Disorders, HCV, and HIV (CHERISH), and Marquette University Clinical Microbiology lab (see descriptions in the Facilities and Resources section). Importantly, for an implementation trial, it is recommended that there is a "firewall" between the staff implementing each strategy so that impacts and costs can be clearly assigned.[129] We achieve this "firewall" by organizing **project teams** with expertise and resources for distinct components of the study. This includes a **technology team** led by PI Mustanski (deliver/support technology across arms); a **CBO team** led by Co-I and former Deputy Commissioner of Public Health Benbow; a **DTC team** led by Co-I Macapagal; and a **methodology team** co-led by Co-Is Brown (implementation science), Schackman (health economics), and Janulis (statistics). See budget justification for an organizational chart of investigators. Our research team is rounded out by **consultants and advisory boards:** Sullivan (expert in MSM HIV geospatial epidemiology and at-home testing), Parsons (expert in creating engaging media for MSM HIV interventions), and Levine (pioneer in applications of eHealth to sexual health). We will draw from the Third Coast CFAR Community Collaboration Board to act as community advisors on all aspects of the project and the Institute for Sexual and Gender Minority Health and Wellbeing's (ISGMH) Youth Advisory Council for YMSM perspectives during the project. We emphasize our collaboration with Hologic, the manufacturer of the widely used Aptima STI tests, who has agreed to cover the costs of all STI tests in the DTC arm, and the CDC Divisions of HIV Prevention (see letters of support).

C.2. Preliminary studies inform our design and demonstrate our capacity to achieve proposed aims.

a. Experience conducting cohort research with YMSM. Project Q2 (PI: Mustanski; N = 248) and Crew 450 (R01DA025548; PIs: Mustanski & Garofalo; N = 450) were cohort studies of LGBT youth and YMSM, respectively. At baseline, participants in each study were ages 16-20 and the samples were extremely ethnically diverse (86% and 82% racial/ethnic minorities). Using retention procedures similar to those in the proposed grant, we achieved 91% and 85% retention at the one year follow-up assessments[130-134] (plus 82% retention at Q2 5-year follow-up).[135] In Crew 450, HIV prevalence at enrollment was 7.8% (58% of these were newly diagnosed in the context of the study), and annual incidence was estimated at 4.1%.[39] YMSM from Project Q2, Crew 450, and a newly recruited sample are now part of **RADAR** (U01DA036939; PI: Mustanski; N = 1,350), a longitudinal cohort study of YMSM ages 16–29 examining multilevel influences on substance use and HIV that has excellent retention rates (89% at 6M, 84% at 12M). This cohort can provide key information to supplement national HIV surveillance data for our models of HIV risk and prevention (see C7f). Furthermore, these cohort studies demonstrate Dr. Mustanski's extensive experience with recruiting and retaining diverse YMSM in HIV research.

b. Experience conducting eHealth HIV-prevention intervention research with YMSM. PI Mustanski and his team have a long history of studying the influence of technology on the sexual health of YMSM,[1, 136-141] including numerous intervention studies (e.g., Queer Sex Ed[142], eDAPT[143], SMART[144], Guy2Guy[145]). These projects have demonstrated the team's ability to create and deliver engaging eHealth interventions, recruit diverse samples (mean of 50% racial minorities across studies), and achieve excellent retention (mean 85%).

C.3. Evidence of efficacy and effectiveness for the KIU! eHealth HIV-prevention intervention for YMSM. KIU! is an online HIV-prevention intervention developed for high-risk YMSM who had recently received a negative HIV test result with the goal of *keeping up* their HIV negative status. Content components were developed in collaboration with YMSM-serving CBOs and subjected to usability testing with diverse YMSM.[12] Extensive mixed-methods research with diverse YMSM also informed the content and ensured that messaging was appealing across racial/ethnic groups.[138] In addition to theoretical grounding in the Information-Motivation-Behavioral Skills model,[146, 147] eLearning

principles[148] guided the development of highly interactive, engaging, and culturally relevant health messages. Several meta-analyses have identified key features of HIV prevention programs[90, 149-151] that are addressed in KIU!, including interpersonal/communication skills training, varied presentation formats, intervention delivery across more than one session, and avoidance of formats that allow participants to meet offline. KIU! involves 7 modules completed across 3 sessions done at least 24 hours apart, totaling ~2 hours of main content, plus 2 booster sessions at 3 and 6 months. Each module is based on a particular setting or situation relevant to the lives of YMSM (e.g., connecting to gay community, meeting guys through apps, dating), with developmentally appropriate behavior-change content embedded within these settings. Across the modules, KIU! uses diverse delivery methods (e.g. videos, animation, games) to address gaps in HIV knowledge, motivate safer behaviors, teach behavioral skills, and instill self-efficacy for preventive behaviors. A description of each module can be found in Appendix 1: Intervention Manual. Below we describe our iterative evaluation of the KIU! intervention.

KIU! 1.0 (R34MH079714) was tested in 102 YMSM aged 18–24 in a pilot RCT designed to assess feasibility, acceptability, and preliminary intervention effects.[12] Analytics related to engagement found high fidelity to intervention and control conditions. Retention was excellent through the 3-month follow-up (87%). Ratings on the Intervention Acceptability Scale were very high.[152] At the 3-month follow-up, the KIU! arm had a significant 44% lower rate of condomless anal sex compared to the control arm (3.7 versus 6.2; *OR* = 0.56, $p < .05$).[12] HIV knowledge and condom intentions increased in both arms, reflecting the fact that the control condition was knowledge-based HIV education. This pattern suggests that both arms had positive effects on attitudinal and knowledge outcomes, but KIU! was significantly better in terms of behavioral outcomes.

KIU! 1.5 was funded by the Chicago Department of Public Health as an HIV prevention service. It was hosted by Northwestern and delivered by a CBO to 579 MSM aged 15–24 through their routine HIV testing programs. An evaluation of KIU! 1.5 (N = 343; 32% Black, 22% Latino) found ratings on the Intervention Acceptability Scale[152] were again very high, and from baseline to 3-month follow-up, there were significant reductions in condom errors ($d = -.32$, $p < .01$), total number of male sex partners ($d = -.34$, $p < .001$), and condomless anal sex ($d = -.2$, $p < .05$).[11, 153, 154] KIU! 1.5 provides important evidence of the feasibility of CBOs integrating KIU! into their routine HIV testing with YMSM without a reduction in effectiveness, lending credibility to our proposed CBO implementation strategy.

KIU! 2.0 (R01DA035145) was a recently completed RCT with 901 YMSM aged 18–29 comparing KIU! to an HIV knowledge control arm, with biomedical outcomes.[155] Participants were enrolled by CBOs, health department clinics, and university centers in three cities (Atlanta, Chicago, New York) and through a national online recruitment campaign involving at-home HIV testing. In addition to behavioral assessments, all participants were mailed at-home STI test kits for self-collected urine and rectal swab samples. The trial reached a high risk sample; at enrollment, participants reported high rates of engagement in condomless anal sex and drug use[156] and STI diagnoses were 13%.[49] Retention in both KIU! and control conditions was high for those enrolled online and through CBOs (>80% for survey and STI tests). Intervention acceptability at completion was again extremely high across racial/ethnic groups included in the study (scaled 1 to 4; API = 3.52; Black = 3.62; Latino = 3.51; White = 3.46, with no significant pairwise differences). At 12 months post intervention, both arms indicated declines in recent condomless anal sex, with a small but significant difference favoring KIU! (control arm declined from 69% to 44%; KIU! arm declined from 68% to 37%; prevalence ratio = 0.83, $p = .04$).[155, 157] At 12-month follow-up, STI rates were significantly lower by 40% in the KIU! arm (control = 14.4%; KIU! = 8.6%; RR = .60, $p < .01$). PrEP became FDA approved during the course of the KIU! 2.0 trial, and while we rapidly added educational material about PrEP, the trial could not test effects on PrEP uptake as it was added mid-course. These results are currently under revised resubmission for publication[14] and have been presented to the CDC[157] with plans for inclusion in the *Compendium of Evidence-Based Interventions.*[50] This RCT demonstrates not only the efficacy of KIU! among YMSM but also the effectiveness of online enrollment and the acceptability and feasibility of at-home HIV/STI testing as part of an eHealth strategy.

C.4. In addition to our completed studies, we conducted additional **formative research** specifically to inform the current proposal:

(a) Qualitative interviews were conducted with 13 key stakeholders from CBOs located across the country (MS, CA, NY, IL, DC, PR). These in-depth interviews focused on questions about their experience with eHealth, their perceptions about its importance for HIV services and client-specific health problems, and barriers for eHealth implementation. Interviews were recorded and transcribed. Two staff independently coded the transcriptions for emergent major themes.[158] Organizations reported some

experience with technology, ranging from as little as a website to building/deploying apps and social media outreach. None of the organizations felt they had the technical capacity to host/support a complex eHealth application but felt confident they could engage participants into a program as long as it had a high degree of usability/acceptability for participants. Organizations felt it was important for them to customize some aspects of the eHealth program to match their brand and population (e.g., including their logo, selecting welcome videos that match demographics of population). Most discussed the importance for dedicated funding to support time for their staff to manage the technology (e.g., "…*people who are doing social media are not the people who are trained for it, and they're not trained for it because there isn't enough in the funding pool to give people or to hire someone specifically for social media*"). Several CBO staff also mentioned the value of assessing areas of needs (e.g., addiction) during program surveys and, with the participant's consent, providing that information back to CBO staff who can then help engage the participant in these services.

(b) We hosted a discussion with 6 health departments about the viability of our implementation strategies. All were very excited about the results of the KIU! 2.0 trial and generated practical ideas for how KIU! could be funded through their existing approaches under the CBO or DTC strategy. An important discussion was around how much funding a CBO would need to implement KIU! to cover staff time. Analysis of contact logs generated in the KIU! 2.0 trial show that, in addition to automated reminder emails/texts, on average 1 human contact occurred for each milestone (e.g., reminder to complete booster session). Based on annual participant flow at CBOs, we project this would represent about a 30% FTE of a health educator or HIV test counselor.

(c) We discussed the study plan with the Third Coast CFAR Community Collaboration Board. The Board provided feedback on the study design and agreed to serve as our community board for the KIU! 3.0 implementation trial (e.g., promote CBO RFA through their networks, staff feedback on CBO dashboard; see letter of support from CFAR).

(d) We visited the CDC Division of HIV Prevention to present on the results of the KIU! 2.0 trial and receive feedback on our implementation strategies. There was much enthusiasm for the need to study the implementation of HIV eHealth programs, and both of our proposed implementation strategies were described as highly feasible under current funding approaches. The CDC agreed to collaborate on the proposed study (see letters of support from Dr. Purcell).

C.5. Study overview. We propose a type III hybrid implementation-effectiveness trial[19] to evaluate and compare two pragmatic strategies for implementing KIU! (CBO versus DTC). In this quasi-experimental trial[119], KIU will be delivered using Strategy 1 (CBOs) in 22 counties for two years; simultaneously, we will delivery KIU nationally using Strategy 2 (DTC). Outcomes will be collected at the level of the YMSM participant (demographics, risk behaviors over time, STIs at baseline and 12 weeks, engagement with intervention); the technology center (cost for development, support, updating); and the CBO level (cost for delivery, CFIR characteristics that explain variability in implementation success).

Eligibility criteria for YMSM will be: speak/read English, age 18–34 years, recently received an HIV negative test result or self-report a negative or unknown HIV status. Participants in the DTC arm will also have the option to submit HIV test results received within the past 3 months. If a participant has a personal copy of their HIV test result they would like to share, the study team will email the participant a link to upload it to the secure REDCap study tracker database. If a participant would like their healthcare provider to share a copy of their HIV test result, the study team will ask the participant to sign a medical record release authorization form to authorize their healthcare provider to share their HIV test results with the study team. We will allow the same processes (i.e., uploading results or authorizing medical record release) for STI test results. In this trial, we add an exclusion criterion that they have not been on PrEP and adherent for 6 months prior, given our goals of reducing HIV risk among those at risk.

YMSM who previously registered for the DTC arm of the intervention but were ineligible due to county restrictions will be notified of changes to study eligibility criteria and emailed a link to complete the baseline survey to determine their eligibility and join the study. Similarly, YMSM who previously completed the baseline survey and screened as ineligible will be notified of changes to eligibility criteria and sent a link to complete the baseline survey again to reassess their eligibility. These YMSM will also be notified of changes to study design (e.g., follow-up schedule) and incentives.

Year 1 will be dedicated to upgrading the KIU! platform, refreshing content to match the current technology landscape and more fully integrating PrEP messaging. We will also issue the RFA for CBOs and select implementation sites. Years 2–4 will be dedicated to the delivery of KIU! and collection of outcome data. Year 5 will be dedicated to the exploration of sustainability and dissemination of study findings. The trial is composed of two components: (1) the service project, i.e. the delivery of the KIU! intervention and booster content and (2) outcome data collection, i.e. the online research surveys that will be used to help us determine the effectiveness of the intervention as it is scaled up. After completing the baseline survey, all participants will be allowed to access the service project components (e.g. KIU! intervention and boosters) regardless of meeting eligibility criteria. In addition, participants meeting eligibility criteria for both components will be able to access all service project components regardless of if they complete the research surveys. Alternately, participants eligible for both components can complete the research surveys but not the service project components (see C.7c. KIU! intervention delivery).

C.6. KIU! platform. The technology platform is a critical aspect of an eHealth intervention because it defines scalability, accessibility, and the capacity to update as new technology emerges.[8] We will embed our intervention within PURPLE: a modular system developed at Northwestern's Center for Behavioral Intervention Technologies (CBITs) for deploying eHealth interventions.[159] PURPLE has been widely utilized for eHealth among diverse populations,[160-164] including YMSM,[165] in >20 NIH funded projects. It is open source, and the final product can be disseminated without the restrictions that often accompany commercial software. Ongoing development, extensive support, and ongoing investment ensure that it will be the platform to use not just today but also well into the future. In order to ensure an exceptional experience by both YMSM and staff users, we made the following technology design decisions for this implementation trial:

(a) Tiered accounts will link YMSM users to a CBO to allow staff to track the progress of their own YMSM participants. A user-friendly **dashboard** will include reports (e.g., enrollment rates, demographics), flags for participants who have not completed KIU! milestones, and a system to log communications with participants.

(b) In our interviews, CBOs expressed a strong desire for some local content. A counterbalance to too much adaptation is the need to maintain fidelity to the core elements of the intervention.[166, 167] As such, we will allow CBOs to configure elements that are specific to their community but not alter core intervention content. **A configuration wizard** will allow CBOs upload their logo, embed information about their organization's services (e.g., hours for HIV testing, PrEP assistance programs), tailor reminder message content, and select from a library of welcome videos that best resonate with their community. CBOs have asked for the ability to assess areas of need (e.g., addiction treatment, housing services, etc.) in KIU! assessments. Given the syndemic of health issues linked to HIV in YMSM,[168-172] this is an important opportunity to link YMSM to needed services. We will enable the option for CBOs to specify services, and, with YMSM consent, will feed requests for services back to the CBO. For the DTC strategy, we will embed geocoded service locators, which we have integrated into past eHealth interventions and found that, in concert with intervention content, they increase use of local services.[173]

(c) Content will be delivered over the Internet as a hosted web application (webapp) and therefore **accessible on a range of devices** (e.g., computer, tablet, mobile phone) due to its *mobile-web responsive design*.[174] This reduces barriers to engagement, particularly for minority YMSM who may access the internet on a smartphone.[175] The design automatically modifies layout of website content to enhance the appearance and usability for each device. At the same time, this design does not require the development of an offline installable app that needs to be programmed for each type of phone (e.g., iPhone, Android) and model (e.g., large versus small screen size), therefore making the intervention more cost-effective and updatable.

(d) Strategy for maintenance: There is no option to freeze eHealth interventions during a trial, as is done in a classic RCT, because failing to address software/hardware updates relegates it to increasing dysfunction and irrelevance.[165, 176] This is a very important difference in implementation for eHealth interventions compared to the classic Diffusion of Evidence Based Intervention model.[177] Furthermore, HIV prevention options have recently expanded and are expected to continue to proliferate (e.g., injectable PrEP), which will require updates to content. Our PURPLE software was engineered to allow updates, and the KIU! content is explicitly designed to rapidly accommodate new information because it was designed with updatability in mind (e.g., stable information like communication within relationships is conveyed through soap

opera style videos; facts about prevention options are conveyed through easily updatable interactive components). Our approach to making these updates will utilize Mohr's principle[176] for optimizing an eHealth intervention during evaluation by: **(1)** identifying behavioral strategies that underlie change (e.g., goal setting, peer norms) and instantiation components (e.g., role model stories) that will not change during the trial; **(2)** monitoring user support logs and regularly testing intervention content for compatibility issues; **(3)** using decision rules to guide content and platform changes (e.g. bug fixes will be implemented immediately, but larger feature changes will be considered by the investigative team by asking if the change interfere with the primary principle being tested and the consequence of not making the change;[176] **(4)** considering the need for usability testing; **(5)** documenting and describing all feature changes as part of the intervention description; and **(6)** Ensuring updates do not compromise our comparisons of implementation strategies because both arms will always receive the same, updated KIU! simultaneously during the trial. Because the content is likely to have modest variability over time, though its principles will remain the same,[176] it is important for us to include measures of effectiveness (e.g., STIs) in this hybrid trial.[19]

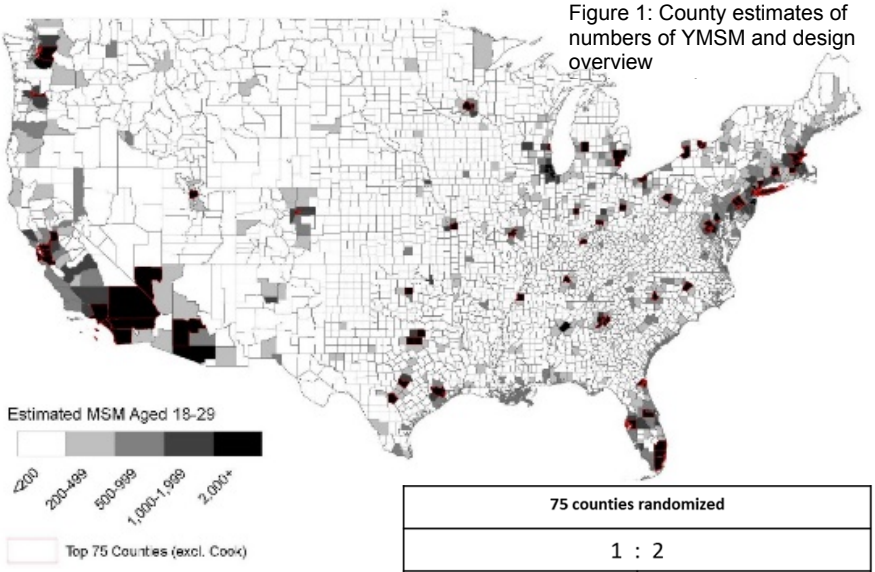
C.7. Design for Aim 1: Compare two implementation strategies using a quasi-experimental trial.
Justification for a type III hybrid implementation-effectiveness design: This approach is designed to compare the impact of two implementation strategies while also gathering data on effectiveness and is recommended when: there is strong evidence for the effectiveness of the intervention (see C3), a strong basis for believing the implementation strategies are feasible and supportable (see C3 and C4), and strong "implementation momentum."[19] In type III hybrid trials, there is no untreated control group because effectiveness has already been demonstrated; the primary question is which strategy works better in facilitating implementation, and effectiveness can be presumed if the observed rates of health outcomes (e.g., STI rates) are comparable to those found in the effectiveness trial.[19] We believe a hybrid trial is warranted, rather than a pure implementation trial, because of the value of ongoing assessment of effectiveness at the individual level as the intervention evolves and is "scaled out."[178] Such trials are inherently pragmatic, and all decisions made about the design of this study started with the question: *How would this work when implemented in the real world?* For example, we questioned having the KIU! intervention hosted and supported at Northwestern CBITs but ultimately decided it was the most pragmatic approach because: few CBOs have the IT infrastructure to locally host an eHealth intervention, our consultation with the CDC suggested it was realistic for a single organization (including a university) to deliver eHealth interventions nationally (see example[179]), and CBITs has a track record of technology transfer to Health 2.0 businesses and could support that option if it is ultimately deemed the best strategy.

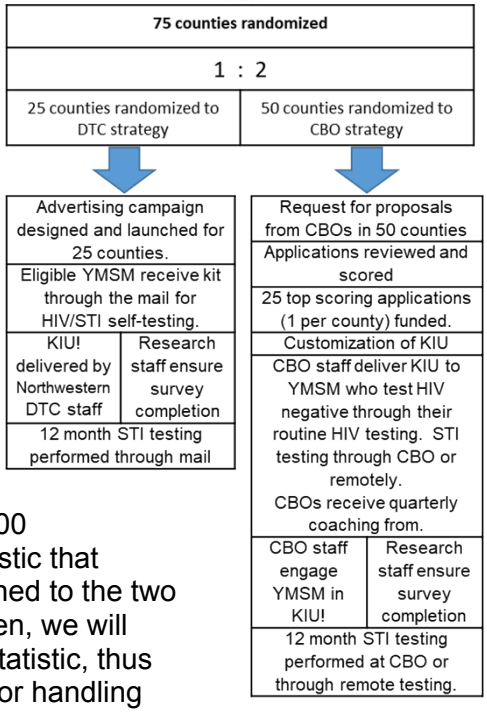
C.7a. Justification for a cluster randomized trial and randomizing counties. In type III hybrid designs randomization occurs at the level of units within service organizations (e.g., CBOs) rather than individuals.[180] This design required a unit of randomization that was functional for both the CBO and DTC strategy. We considered randomizing to states, but they were too large of a region to effectively measure implementation outcomes and control for variability in key factors. We considered randomizing CBOs that were willing to implement but decided it was unethical to ask CBOs to apply to an RFA only to have their region randomized to a DTC approach. We considered randomizing at the city level, but estimates of YMSM are not available at the city level; the smallest available unit is counties. We ultimately selected randomization at the county level because of its advantages as a geographic and administrative region.

As of January 2021, KIU will be delivered using Strategy 1 (CBOs) in 22 counties for two years; simultaneously, we will delivery KIU nationally using Strategy 2 (DTC). YMSM participants in the DTC strategy will be matched to CBO strategy participants based on post-hoc propensity scores.

C.7b. Selection of counties and randomization. In order to select counties, we will use the following inclusion/exclusion criteria: **(1)** The county's estimated number of MSM between the ages of 18–29 is at or above 2,000 based on an Emory age-adjusted estimate of MSM population sizes at the county level[16] (N = 92 counties). We will work with Consultant Sullivan (expert in HIV and MSM spatial epidemiology) to consider if some counties should be merged in cases where a single metropolitan area includes multiple counties. **(2)** The county's 2013 HIV prevalence case count among MSM is at or above the national median. **(3)** At least one CBO that provides HIV testing exists in the county. **(4)** We will exclude counties that have already used KIU! in previous studies (e.g., Chicago's Cook County). From this, a random sample of 75 counties will be selected and randomized 2:1 to the CBO and DTC strategies. Power analyses indicate 50 total counties are necessary to achieve our aims (see C7g). We will randomize 50 to the CBO strategy because we expect that, despite our plans for intensive outreach to health departments and CBOs in the selected counties, some will not have CBOs that apply or are ultimately qualified for selection to implement KIU!. Therefore, randomizing 50 will allow us to meet our goal of 25 counties implementing the CBO strategy. We will randomize 25 counties to receive the KIU! DTC strategy because we expect no selection loss[181] from counties where we will advertise online directly to YMSM (see figure 1 and analysis section). As of January 2021, the KIU! DTC strategy will not be limited to these randomized counties. The KIU! DTC strategy will expand to a nationwide catchment area. In addition, only 22 counties were randomized to the CBO arm due to grant budget cuts. Our randomization procedure will guarantee as much balance as possible on 5 major site attributes—level of urbanicity, region of the country, HIV prevalence, racial/ethnic diversity, and county/municipality. Following procedures we have used in two previous implementation trials that randomized at the county level,[182] we will use simulation to generate 10,000 potential assignments. For each we will compute a Hotelling's T^2 test statistic that measures how far apart the multivariate means are for the counties assigned to the two implementation strategies across major site attributes listed above.[183] Then, we will randomly select one assignment that is within 2% of the smallest T^2 test statistic, thus ensuring nearly optimal balance across all attributes. See analysis plans for handling potential selection bias. Because reach is a primary outcome of the trial we do not pre-specify how many YMSM will participate, however we anticipate 315 participants enrolled in the CBO arm and 800 participants enrolled in the DTC arm.

Figure 1: County estimates of numbers of YMSM and design overview





C.7c. KIU! intervention delivery. Figure 1 illustrates the flow of intervention delivery and data collection from randomization of counties through data collection. As recommended for implementation trials,[129] there will be a "firewall" between roles and activities related to KIU! intervention delivery and outcome data collection (i.e., recruitment and KIU! delivery will be done by CBO staff or staff on the Northwestern DTC team, but collection of outcome data will be managed by methodology team staff for both strategies). This assures that a YMSM could drop out of the KIU! intervention but still be tracked for outcome data collection, consistent with the intention-to-treat principle.[184] Intensive efforts will be put into tracking and retaining participants by research staff using procedures proven effective in our previous online and offline studies (e.g., contact trace protocol,

automated and personalized reminders, and use public databases such as LexisNexis for updated contact information). Given this is an implementation-focused trial it would be inappropriate to pay YMSM for research data collection in a way that would bias assessment of implementation outcomes (i.e., enrollment in KIU! is driven by research payments). At the same time, participants deserve some token for their completion of data collection. As a compromise, we will enter eligible participants who complete surveys into a monthly raffle to receive a $200 pre-loaded Visa gift card.

Intervention delivery will be very similar across both strategies, which always begins with an HIV negative test result or self-reported HIV status of negative or unknown. Those who meet other eligibility criteria (e.g. age, gender, county) will still be encouraged to complete an HIV test to confirm their status. Participation in the study, however, will no longer be contingent on a confirmed HIV negative result. Participants will receive the 3 sessions of KIU! Participants can complete all 3 sessions in one sitting but will have a maximum of 3 weeks to complete the sessions. Booster sessions will be delivered at 6 and 12 weeks following completion of the main content, and follow-up survey data collected at 12 weeks. Outcome assessments always occur before boosters but participants will have the option to skip past the assessments without completing them.

Participants who enrolled in the study when the original follow-up schedule was in place (i.e., at 3-months, 6-months, and 12-months) will be notified of the changes to the follow-up schedule and only have data collected at 12-weeks. If the participant is already beyond the 12-week follow-up window, the study team will still administer this final follow-up survey and adjust for differences in time of data collection during data analysis. DTC participants enrolled under the original follow-up schedule will also still be shipped a follow-up STI test kit for completion. DTC participants will also be notified of and receive new incentives following intervention and follow-up completion. Templates for these email notifications is included in the document "Study Changes & Incentives Notification Email" uploaded to the IRB portal. Participants in the CBO arm of the study will be notified of the changes by CBO staff following their preferred internal protocols and procedures.

C.7d. CBO implementation strategy. CBO Identification and Recruitment: CBOs will be selected through a Request for Proposal (RFP) process. The RFP will describe research and KIU! delivery activities to be conducted as part of the study and allowable budget to carry out the activities. To maximize the number of CBO applications, we will broadly disseminate the RFP through health departments, national organizations (e.g., NMAC, NASTAD), and direct outreach to CBOs. The RFP will ask CBOs to describe their past experience providing HIV services for YMSM, including: recruitment strategies for HIV testing; STI screening services; description of prevention and care services offered in-house and description of referral process to external HIV prevention and care services; number of YMSM tested for HIV and other STIs and percent testing positive in the previous calendar year; service catchment area; and number of staff conducting HIV services. Applications will be reviewed using a review panel and scored using procedures Co-I Benbow implemented while Deputy Commissioner of Chicago Public Health, with 25 highest scoring CBOs (one per county) selected. Funding from this grant to CBOs will be capped at $20,000 per year during the 2 years of implementation. This value was derived from our 30% FTE estimate for implementation of KIU! in routine HIV testing (see C4). It is expected that in many cases, CBOs will supplement this budget with in-kind or resources from other sources, as is often the case. We will capture this information in the cost analysis (see C7f).

CBO Participant Recruitment: Our anticipation is that CBOs will recruit participants to Keep It Up! in a variety of ways - from onsite HIV testing to outreach events to social media. At its core, however, referral and initial registration will take place during or immediately following the administration of an HIV test which has returned a non-reactive (negative) result. CBO recruiters will inform their clients who fit the requisite categories for age range, sexual risk, and gender of the opportunity to enroll in Keep It Up!. For those who are interested in enrolling, CBO staff will register them for the program by creating an account for them in the Keep It Up! system. An automated email will be sent to the participant to confirm their account. After the participant has confirmed their account, they will be directed to the online consent and baseline survey that includes questions to verify their eligibility. Following this, the CBO's involvement turns to retention, wherein, through varied means and strategies, CBO staff will work with their enrolled clients to complete the intervention.

CBO Training: Under supervision of Co-I Benbow, project staff will provide initial online training courses to CBO staff on ways to promote HIV testing with diverse YMSM, use of the KIU! technology platform, how to integrate KIU! into routine HIV testing, and how to track/retain participants in HIV prevention services. CBOs will also participate in a hands-on practice session using the KIU! technology. The training courses will incorporate group video-trainings and webinars for staff members at each CBO. One-on-one trainings via

video-conferencing will be offered for CBOs who require further training or as challenges arise. A forum connected to the training site will also provide staff across CBO sites with the opportunity to collaborate together throughout the project. For example, they will be able to identify mutual challenges to implementation, and to develop solutions together. We believe that these online training activities for CBO staff are best described as Program Evaluation/Quality Assurance Review/Quality Improvement Project or Course-Related Activity rather than Human Research and will therefore not regard CBO staff as study participants.

Data related to the training courses will be collected and linked to each CBO. No PHI will be collected from CBO staff. Metrics that will be collected include course progress, quiz performance (number of attempts and score), time spent on a course, and responses to questionnaires on topics such as staff readiness and attitudes about the intervention. All data will be related to CBO staff implementation of the intervention. Data will be analyzed on an aggregate level to better understand overall how well CBOs are learning to implement the intervention. For example, we may look at average quiz scores of staff from a CBO or the average amount of time staff members spent on the training as a way to investigate any associations between level of engagement with the course and successful implementation of Keep It Up!.

Data will be pulled directly from the KIU! platform that houses the training courses. Access to the course will require staff and supervisors to log in using their unique credentials. Likewise, individuals who are not involved with the CBO arm of the study will not have access to online training.

Northwestern research staff will be responsible for monitoring CBO staff progress as well as group interactions on the forum throughout the duration of the study. Northwestern staff will use email addresses provided by the CBO to communicate with CBO staff to complete elements of the training. Northwestern research staff will also follow up with phone call and individual email reminders if CBO staff are non-responsive to the emails or require assistance with accessing training.

C.7e. DTC strategy. Recruitment: YMSM will be recruited nationally online via paid social media advertising (e.g., Facebook, Instagram). As we have done in prior studies, advertisements will target placements by age, gender, sexual orientation, racial background, “likes” that are relevant to YMSM (e.g., local LGBT organizations, “out” celebrities), and location (i.e., target county). YMSM who click the ad will be routed to a landing page on the KIU! program website where they can self-register for the program. They will provide their name, phone number, email address, and county. They will also be able to click checkboxes to indicate if it is okay to contact them by text message and leave voicemails.

YMSM who live in a county that is eligible for the CBO arm of the program will not be allowed to complete registration for the website. They will be told that the DTC version of KIU! is unavailable in their county but that it may be available through a local organization near them. These participants are not allowed to enroll through DTC recruitment strategies because it would confound results by study arm.

YMSM who live in any other county will be allowed to continue the registration process for the website. After filling out the registration form on the landing page, they will be sent an automated email with a link that they must click to confirm their account and set up password information. Once their password has been created, participants will watch a Welcome Video that describes KIU! After participants have watched the Welcome Video, they will be presented with a link to the full online consent form and an online baseline survey which includes questions to assess eligibility for the research component of the program (i.e. follow-up online surveys and free at-home HIV and STI test kits). As above, information collected this way will be encrypted and securely transmitted to the Northwestern server. After completing the survey, all participants will be directed to the intervention content.

To improve recruitment success, we will also pay $50 to participants who meet eligibility criteria for the research component and complete the initial intervention content (first three sessions). Eligible DTC participants will also receive $10 for completing the 6-week follow-up, $20 for completing the 12-week follow-up, and $20 for completing 12-week STI testing.

If the participant meets eligibility criteria for the research components of the program, they will receive at-home HIV and STI test kits and receive follow-up surveys at 12 weeks in addition to having access to the intervention

content (i.e. service project portion of Keep It Up!). These participants will also receive an incentive for completing the initial intervention content (first three sessions) and 6- and 12-week follow-up.

If the participant does not meet eligibility criteria for the research components of the program, they will not receive at-home HIV and STI test kits, incentives, or follow-up surveys at 12 weeks. They will, however, continue to have access the intervention content (i.e. service project portion of Keep It Up!).

As of January 2021, participants who did not meet the original eligibility criteria (e.g., 18 – 29, CAS in past 6 months, living in specific DTC county) for the research components of the study but went on to complete the intervention content will be enrolled into the study if they meet the new eligibility criteria. The study team will review their baseline survey data to assess eligibility. They will be notified of the new follow-up schedule and incentives for 6- and 12-week follow-up. These participants will receive an incentive for completing 6- and 12-week follow-up. They will also receive a follow-up at-home STI test kit.

Additionally, RAs will send private messages to young men on social media sites who “like” or “share” the ads that we post. These messages will encourage the young men to click the link in the ad sign up (i.e. register) for the program if they have not already done so. Samples of the messages we will use are included in the “Online Recruitment Ad Samples” document. The live ad campaigns will be continuously updated with similar photos and text at the research team’s discretion in order to optimize the campaigns. The study team may also use short video clips or gifs with similar imagery in ad campaigns as these formats perform well in online ads. Dating/sex-seeking apps (e.g., Grindr) will also be used to recruit YMSM, using a similar advertising approach as social media. In addition, we will “tap” or message (e.g., “Hello, my name is [] and I work on a research study called Keep It Up! Would you like to learn more about our study?”) dating app users who appear to fit our eligibility criteria based on information in their user profile and note in their profiles that they are open to contacts that are not sexual in nature (e.g. “Looking for Networking” and “Looking for Chatting”). If a user taps us back or sends us a private message in response, we will respond with a message telling them more information about the study and encouraging them to sign up (i.e. register) in the KIU! app. As we have done in prior eHealth studies, we review our campaign quarterly with the ISGMH Youth Advisory Council (comprised of YMSM) to help develop fresh ad content, refine “like”-based targeting strategies, and explore new platforms for advertisement.

Although recruitment of YMSM will primarily occur through the recruitment strategies listed above, they may also be recruited through other sources such as print ads (e.g. flyers and brochures – see “Print Recruitment Ad Samples”) and referrals from staff at local organizations (e.g. university student groups, CBOs, social settings) that study staff forge relationships with, referrals from ongoing studies or IRB approved research participant registries, and friend referrals. We will also collaborate with companies, such as Trialfacts, that have extensive marketing and advertising expertise, and specialize in helping to recruit participants into clinical trials. We will use both online and print ads that use a mix of language that refers to Keep It Up! as an online program/project and language that refers to Keep It Up! as a research project. We do so due to the unique nature of Keep It Up! being both a service project as well as having research components (e.g. online surveys). Despite the variety of language used in the online and print teaser materials, all interested parties will be directed to our online registration landing page that states that the online KIU! program is offered as part of a research study. Costs will be recorded. In order to **avoid fraud** and reduce the likelihood of participants completing the study multiple times, we will enact verification procedures established in our prior online research with YMSM[12, 13, 173, 185-189] and described in the literature.[190-194]

We will supplement these recruitment strategies with snowball recruitment. This sampling technique is often used in hidden populations that are difficult for researchers to access. Enrolled participants who complete the initial three intervention sessions will receive an email asking if they would like to recommend KIU! to their friends. The email will include a link to a data entry form in REDCap where the enrolled participant (“seed”) can enter the email addresses of up to five friends (“sprouts”). Each sprout will receive an automated email that briefly describes KIU!, mentions the seed who provided the referral by name (e.g. “John recently completed an online health program named Keep It Up! and thinks that you may like it too!”), and includes a link to a KIU! registration form in REDCap. The REDCap registration form will automatically capture for internal tracking

purposes the REDCap record ID of the original seed that made the referral. Sprouts will enter their name, email address, and county. Optional elements collected on the page are phone number and a checkbox to indicate if it is okay to contact them by text message. Once the sprout submits the form, background syntax will run to determine preliminary eligibility based on duplicate contact information and eligible county. If a sprout is eligible after completing the REDCap registration form, KIU! DTC staff will register them into the KIU! app. The seed will receive $10 for every sprout who is eligible and completes the baseline survey.

Intervention delivery: All potential participants who complete the registration process and do not live in a CBO eligible county will be given access to the KIU! intervention content. Potential participants will be assessed for eligibility to receive a shipment containing a kit with STI and HIV testing supplies. We currently plan to utilize OraQuick[195] because it is FDA approved for self-testing and has been widely studied for this purpose.[110, 111, 113, 196, 197] During the COVID-19 pandemic, participants will have the option of testing with an Oraquick (oral swab) or Molecular Testing Lab (MTL) (finger stick) kit. Providing testing through MTL will limit the need for Northwestern staff to go into the office during the COVID-19 pandemic to mail out test kits to participants. Participants who opt to do testing through MTL will have a more invasive testing process (i.e. finger prick) and longer wait time for results, but the benefit of having confirmatory testing automatically done on any preliminary positive results so that they do not need to visit a healthcare provider during COVID-19 for confirmatory testing.

As was done in KIU! 2.0 and our other collaborative studies, participants who select the Oraquick test kit will be instructed to take a photo of their test paddle and upload it in REDCap so the result can be confirmed by staff (see Human Subjects for plans for referral to care for HIV positive results).

Participants who complete testing with the MTL kit will be required to mail back their blood specimen to MTL for testing. They will be asked to consent to allowing MTL to share their results with the study team. The study team will be able to access participants' test results on MTL's secure web-based portal. After shipping their blood specimen, participants will receive their results in about a week in one of two ways. Participants who test negative will log into MTL's secure web-based portal to authenticate their identity, view their test results, and download a copy of the results. MTL will not to upload results for participants who test HIV positive. Instead, a study team member will call the participant, verify their identity by asking them to confirm their full name, date of birth, and address, notify them of their positive status, and provide support and linkage to care.

Participants who agree to take either at-home HIV test kit will also receive at-home urethral and rectal STI test kits. Participants who opt to receive the MTL HIV finger prick test will receive STI tests from MTL. They will log into MTL's secure web-based portal to authenticate their identity, view their test results, and download a copy of the results if they wish. Participants who opt to receive the Oraquick oral swab test will receive STI tests donated to the study team by Hologic. They will log into REDCap, authenticate their identity by answering security questions, view their test results, and download a copy of the results if they wish.

Participants who do not complete the at-home HIV test (but self-report a negative or unknown status in the baseline survey) will continue to have access to the KIU! intervention content as well as the online surveys (i.e. research component) and at-home STI test kits at 12 week follow-up now that the study no longer requires confirmed HIV status for enrollment in the DTC arm of the study. These participants will also receive incentives for completing the initial intervention content (first three sessions) and completing the 6- and 12-week follow-ups and testing.

Participants who complete the at-home HIV test and have a negative test result will continue to have access to the KIU! intervention content as well as the online surveys (i.e. research component) and at-home STI test kits at 12 week follow-up. These participants will also receive incentives for completing the initial intervention content (first three sessions) and completing the 6- and 12-week follow-ups and testing.

Participants who complete the at-home HIV test and have a positive result will continue to have access to KIU! intervention content (i.e. service project component) but will not be eligible to complete follow-up surveys or at-home STI test kits at 12 week follow-up. They will also not be eligible to receive incentives.

Participants who upload a negative HIV test result or authorize a healthcare provider to share a negative HIV test result with the study team will continue to have access to the KIU! intervention content as well as the online surveys (i.e. research component) and at-home STI test kits at 12 week follow-up. These participants will also receive an incentive for completing the initial intervention content (first three sessions) and completing the 6- and 12-week follow-ups and testing.

We also recognize that HIV diagnostics are improving and therefore before launching this phase will review best available self-testing options with Consultants Sullivan and Parsons, who, with PI Mustanski, have extensive experience with at-home HIV/STI self-testing.[198-200] STI testing is described below.

Table 1: Application of RE-AIM to KIU! 3.0 implementation trial

Measure	Source
REACH	
Number of YMSM screened for KIU.	Screening logs. Emory CAMP models of YMSM by county.[16]
Proportion of invited YMSM who begin KIU.	Number of study pin codes activated and provided.
Proportion of KIU! participants that are Black or Latino.	YMSM self-report in enrollment survey.
Proportion of KIU! participants with an STI at enrollment.	CBO medical records or self-testing kits.
Proportion of KIU! participants who engaged in unprotected sex (no condom or PrEP) in prior 3 months.	YMSM self-report in enrollment survey.
EFFECTIVENESS	
3-month change in unprotected sex	YMSM self-report at 3-month surveys
Rectal STI incidence at 3 months	CBO EMR or self-test kit
Rate of PrEP initiation over 3 months	YMSM self-report at 3-month surveys
Self-reported change in testing, condom use, and PrEP self-efficacy at 3 months	YMSM self-report at 3-month surveys
ADOPTION **Adoption characteristics are not comparable across arms. Measured differently by arm** See Aim 2.	
IMPLEMENTATION	
Mean number of KIU! modules completed by participants.	System analytics. Metrics of activity within modules.
Intervention Acceptability	YMSM self report at intervention completion points
Cost of intervention delivery per participant	Interviews, study logs, and CBO financial information
Cost of intervention delivery per infection averted	Estimated based on effectiveness and cost.
MAINTENANCE/SUSTAINMENT **Maintenance characteristics are not comparable across arms.**	

C.7f. Aim 2 Outcomes: While implementation science is a relatively new field, there have emerged some standards on how to select and evaluate outcomes from randomized implementation trials to meet priorities of researchers, funders, and service providers,[25, 95] including our own publications.[33, 176, 178, 201-209] By drawing from our formative interviews with the CDC, health departments, and CBOs, we identified 3 characteristics of greatest importance: reach to high risk YMSM, effectiveness at reducing HIV risk among those engaged, and cost for delivery. For this trial, "public health impact" (PHI)[20-22] involves the first two characteristics of (1) absolute # of YMSM who engage with KIU!, weighted by HIV risk (i.e., engagement of YMSM from higher risk communities is valued more), and (2) effectiveness at reducing HIV risk, defined as a composite of self-efficacy to get an HIV test, always use condoms during sex unless on PrEP, and PrEP utilization at 3 months. By measuring individual-level change on these modifiable factors, our index of PHI allows for heterogeneity in response to KIU! across individuals, race and age groups, counties, and implementation condition. Specifically, for each subject *i* in county *c*, let P_{ic} represent estimated HIV prevalence based on the MSM's age and race.[210] Effectiveness is marked by the estimated change in that person's risk for HIV from outcome to baseline, $R_{ic}^1 - R_{ic}^0$, determined by observed changes in target risk behavior: CAS, STIs, and adherent PrEP use, all of which are known to have major impact on HIV transmission in MSM.[48, 211-213] We base our modeling of HIV risk on published single-exposure probabilities[214] and account for multiple exposures using binomial modeling. We define PHI for each county *c* to be summed over individuals' risk group by impact; $PHI_c = \Sigma_i P_{ic} * (R_{ic}^1 - R_{ic}^0)$. Because these are individual-based measures, we will use two-level mixed-effect modeling.[215] Measuring cost is described below, and from these we will compute cost per infection averted, which is analogous to the measure used by CDC to decide which effective HIV prevention intervention would be supported as part of high impact prevention.[23, 24] We recognize that implementation success is a multidimensional construct, and it is common to measure and report multiple outcomes,[25, 95] which increases the significance of an implementation study because stakeholders may differentially value certain metrics (e.g., a funder may set a

ceiling for program cost, a service provider may prioritize effectiveness or reach). As indicated in Table 1, other constructs from the RE-AIM framework[21, 22, 63] will also be assessed and reported to describe critical implementation information (Aim 1).

Consistent with the pragmatic focus of this hybrid trial, collection of **self-report measures from YMSM** will be kept to a minimum (~10 minutes). Measures will be securely collected using REDCap and include: **(1)** demographics (age, race/ethnicity, zip code, sexual orientation identity); **(2)** the HIV Risk Assessment for Sexual Partnerships (H-RASP),[216] which has been used in numerous studies of YMSM[130, 168, 217-229] and was validated against daily diary reports.[230] Sexual behaviors are assessed on a partner-by-partner level, starting with recent partners, with questions differentiating between insertive and receptive anal sex and assessing if condoms or PrEP were used during sex with each partner[231]; **(3)** PrEP use and adherence will be assessed using a measure from our epidemiological research with YMSM[231]; **(4)** HIV testing history; **(5)** intervention acceptability will be assessed by the Treatment Acceptability Rating,[152] adapted for eHealth research[12, 173], which includes open-ended questions (e.g. "What did you like the least?") and closed-ended Likert questions that form a scale of intervention acceptability (alpha = .87). Demographics will be assessed at baseline and acceptability at intervention completion. Measures of HIV risk and preventive behaviors will be collected at baseline and at 12 weeks post-intervention.

STI testing: Rectal and urethral STI incidence was a primary outcome of the KIU! 2.0 trial,[13, 14, 157] and therefore, it is important to include this measure as we seek to assess KIU! effectiveness as it is scaled out (i.e., does effectiveness drop in wider-scale implementation?). The convenience of receiving rectal/urethral STI testing through kits shipped to their homes was a described as a major benefit by participating in the KIU! 2.0 trial.[232] That, coupled with the high rate of STIs among YMSM[49] and their effect of increasing transmission of HIV due to increased biological susceptibility,[233, 234] justifies our inclusion of STI testing as part of the core KIU! "package" of intervention activities. We will test for STIs again at 12-week follow-up as a research activity and include results as a component of our PHI outcome. Because of its importance to our PHI outcome, we will incentivize the completion of 12-week STI testing. DTC participants and CBO participants who complete at-home STI testing at 12-weeks will receive a $20 gift card. CBOs participants who complete 12-week STI testing onsite at a CBO will be compensated according to established CBO internal guidelines for providing participants with incentives for participating in prevention activities. Our inclusion of PrEP use in the calculation of the PHI outcome is important as there is a debate in the field about whether PrEP initiation results in higher STI rates.[235-238] We emphasize that Hologic, Inc. has covered the cost of STI testing in this implementation study, making it financially possible to include as an outcome in a study of this scale. We will include standard costs of STI testing at baseline as part of the KIU! "package" in our cost estimates. We propose to test for rectal and urethral Gonorrhea (NG) and Chlamydia (CT) because: (1) they are the most common STIs among young adults in the US[44]; (2) they are the principal STIs that amplify HIV infection among MSM in the US[239]; and (3) there are established solutions for distance screening.[240]

In the CBO strategy, STI testing will occur in person along with HIV testing. Ability to perform STI testing will be prioritized when selecting CBOs in the RFA. YMSM will be asked to sign a medical record release authorization form and agree to have their HIV and STI test results shared with researchers. CBOs will have the option to use their own local version of the medical record release form if preferred to the release form provided by the KIU! study team. Hologic, Inc is a collaborator on this proposal and has offered to provide technical assistance and provider trainings on implementing rectal STI testing as needed by CBOs (see letter of support). For CBOs that do not have the capacity for STI testing but are otherwise highly competitive in the RFA process, we will either have CBO staff collect samples on site and ship to our testing lab, or we will ship collection kits directly to YMSM (as in the DTC strategy). To determine which CBO participants have not received STI testing at registration, we will ask CBO staff to declare whether a newly registered participant has received or will receive the required STI testing. If a newly registered participant has not and will not receive STI testing, we will offer to mail STI test kits to participants, with their consent. When participants complete the medical release for their HIV/STI test results, they will be asked for consent to having STI tests mailed to their homes in the event that either their CBO did not perform the tests or they do not consent to their CBO providing the results. Participants will be encouraged by research staff at Northwestern to return to the CBO for STI testing at the 12-week follow-up point, and participants who decline to do so will be shipped at-home STI kits as in the DTC strategy. STI testing at 12-week follow-up is for the research component of the intervention and will therefore be optional for all participants. The CBOs that participants can visit for repeat

STI testing are sites that offer testing as a part of their regular services. In addition, CBO providers would be following the CDC recommended schedule for annual STI testing among YMSM.

A Northwestern KIU Data Manager will regularly export a REDCap report of all participants who have consented to have their STI results shared with NU by their CBO. These reports will be generated via completions of a separate REDCap Participant survey, which begins with an online consent form that participants must agree to before completing the survey. Only the data managers will have access to KIU REDCap projects and the data collected therein. This report will be exported periodically to ensure CBO's are able to report results in a timely manner and for a reasonable number of participants. The exact timeframe and number of participants will be determined after the study launch, as we will have a better sense of how quickly CBOs are consenting participants. Only participants who have consented, but whose results NU has not yet received, will be included in the REDCap report to be exported.

Once exported, the data manager will run a pre-written code that will do two things: (1) match participants to their corresponding CBO and (2) import this participant information (name, date of birth) into surveys designated for each CBO. Automating this process will prevent human error. Participant information imported into the survey will be read-only. These survey links then will be emailed to a designated staff person at each CBO. REDCap emails are a secure method of data transfer, and the survey itself is accessed via a secure webpage. A designated CBO staff person will enter the following information for each listed participant: date of testing, and test results for the following: rectal chlamydia, rectal gonorrhea, urethral chlamydia, and urethral gonorrhea. There is one page for each participant. CBOs will not be able to enter any data for participants for whom NU did not request results, ensuring NU only receives STI data from consented participants. When finished, the CBO staff member will "submit" the survey and the data will be securely transferred to NU.

In the DTC strategy, we will use the same approach as the KIU! 2.0 trial that produced a >90% return rate.[13] YMSM are mailed urine and rectal swab collection kits in a nondescript box at baseline (with an at-home HIV test) and 12 weeks. Written and video instructions for collecting and returning the samples are provided with a pre-paid shipping container to return specimens. Results will be available within 3 – 5 business days of kit arrival. Testing for samples collected with Hologic collection kits will performed using the widely used (89% market share) FDA-approved Gen-Probe APTIMA Combo 2® Assay on the Panther system.[241] After STI test results are received by the DTC team, they will be delivered to participants through a secure website. Participants will be able to print a hard copy of their results with an explanatory cover letter. Testing for samples collection with MTL BD ProbeTec Chlamydia trachomatis/Neisseria gonorrhoeae (CT/GC) Qx specimen collection kits will be performed using the BD ProbeTec CT/GC Qx Amplified DNA Assays on the BD Viper and Roche 4800 systems. Participants will log into MTL secure online portal to view and print a hard copy of their results. Study staff will also be able to view participant results by logging into the secure online portal. HIV testing of dried blood spots specimens provided by MTL will be performed using the Geenius™ HIV 1/2 Supplemental Assay on the GS HIV Combo Ag/Ab EIA system. If positive test results arise, study staff will provide local referrals for free or low-cost treatment and make a legally required confidential report to the appropriate health department (see Human Subjects).

Participants in the DTC arm will also have the option to submit STI test results received within the past 3 months. If a participant has a personal copy of their STI test results they would like to share, the study team will email the participant a link to upload the results to the secure REDCap study tracker database. If a participant would like their healthcare provider to share a copy of their STI test results, the study team will ask the participant to sign a medical record release authorization form to authorize their healthcare provider to share their STI test results with the study team.

Cost data: We will follow established guidelines for collecting cost data and conducting economic evaluations and will conduct cost analyses from the perspective of the healthcare sector.[242-244] We will follow the 3-step micro-costing approach, a technique in which all inputs consumed in an intervention are identified and quantified in detail and then converted into fiscal terms to produce a cost estimate.[245] **(1)** We will describe all resource inputs involved in delivering KIU! for each strategy, excluding research-related resources. The resource categories include: 1) *start-up* (e.g. CBO recruitment, initial training); 2) *variable*, which increase as a direct function of the number of participants (e.g. shipping HIV kits); and 3) *time-dependent*, which do not vary in relation to the number of participants but are used during program operation (e.g. social media advertisements, booster training/technical assistance, staff time, space). **(2)** We will measure the number of units consumed for each of these resources, using study records and interviews with staff for most resources,

including training and client recruitment activities at CBOs. We will supplement these estimates with data that we collect directly from CBOs in surveys conducted by email and by phone. Surveys will collect additional information about resources incurred at the CBO to deliver KIU! such as staff recruitment, time spent with participant engagement, and associated non-personnel and overhead costs. We will pre-test the survey instrument with a convenience sample of CBOs, and we will visit up to 3 sites in person to further refine the instrument and identify additional data collection needs. **(3)** For each resource unit we will determine a value in dollars and then multiply this value by the number of units consumed. These values will represent the cost of the resources required to initiate and deliver KIU! on an ongoing basis. To value personnel time, we will employ national average wage and fringe benefit rates reported by the US Bureau of Labor Statistics[246]. For the exploratory sustainment aim the economic evaluation team will use the micro-costing data to develop a budget Impact Tool that can reflect local site costs.[32]

We will employ the variable and time-dependent costs to estimate cost per participant and cost per infection avoided at one year; start-up costs will be reported separately. To estimate cost per infection avoided, we will develop an estimate of infections avoided based on the effectiveness outcomes observed in the study. First, we will estimate the expected HIV incidence for the study population without any intervention. To do so, we will stratify the study participants by age, sex, race, and county of residence. Working with consultant Sullivan, we will then assemble CDC HIV surveillance reports of age- and race-adjusted HIV incidence in each county. The expected HIV incidence in the KIU! 3.0 study population without any intervention will be calculated as the weighted average of age, race, and county-specific incidence of HIV, where the weights are the relative N of each stratum. Next, we will estimate the HIV incidence for each arm of KIU! 3.0. Because it is not feasible to measure and compare HIV incidence directly, we will leverage STI (GC/CT) incidence data to calculate HIV incidence, adjusting for the fact that PrEP use could affect the relationship between incidence of STIs and incidence of HIV. We will estimate the number of HIV infections in each follow-up period (months 1-3, 4-6, 7-12) as: (the number of STIs) X (incidence rate of HIV among those with STI) X (PrEP initiation rate in that period) X (PrEP protective benefit).[211, 247, 248] The number of HIV infections averted at one year for each study arm will be the difference between the estimated number of HIV infections expected and the estimated number of infections occurring in each study arm.

C.7g. Analytic plan for Aim 1. We will employ Multivariable Generalized Linear Mixed Models (GLMM)[243] for our analyses, as they account for nested individual observations within counties and are commonly used in cluster-randomized trials.[249] The multivariable aspect of the model allows for the control of factors that are unbalanced between arms because they either were not accounted for in the randomization process or may have become unbalanced due to loss to follow-up. To account for potential selection bias in constructing an efficient (1 DF) adjustment for measured differences in county-level covariates, we will adjust for the linear combination forming the first canonical covariate that maximally distinguished the sites in the two arms.[181, 250] Similar to propensity score analysis, we will also formally include the model that predicts selection effects.[121] We will estimate standard errors using nonparametric bootstrapping techniques within the multivariable framework[243] treating arm as a dichotomous indicator. The differences between the intervention arms will be evaluated by examining the statistical significance of the level-2 (i.e., cluster level) dichotomous indicator for the intervention arms. We will estimate and compare the difference in predicted mean cost per participant between the arms, and will also use those estimates of mean cost to characterize the cost per HIV infection averted in each arm of the study. For cost analysis, parametric methods based on parameters obtained from bootstrapping will be used to estimate acceptability curves,[244] which will illustrate the probability that the more expensive intervention is a good value for different willingness-to-pay thresholds (i.e., incremental cost per infection avoided). Finally, all analysis of outcomes will conform to best practices in analysis of randomized trials, including intention-to-treat analysis and sensitivity analysis of missing data and multilevel multiple imputation in order to examine the potential effect of missing responses on the results.[251-253]

Power analysis for primary study outcome. In order to determine power for the PHI outcome measured at the YMSM level, the required number of clusters was estimated using the clusterPower package in R,[254] which accounts for the nested nature of YMSM within clusters. Assuming an intra-class correlation coefficient of up to 0.125 and a continuous outcome, 300 young MSM per cluster will have adequate power (0.83) to detect a small-to-medium effect (d = 0.30) between the two arms with 50 clusters. For our other primary outcome of cost per infection avoided, measured at the cluster level, the power analysis calculated in G*Power[255] indicated that 50 clusters would be sufficient to achieve adequate power (0.85) to observe a

moderate effect size (f^2 = 0.15) using the mixed models described above. Variability in the number of YMSM enrolled per county within a reasonable range (50-300) had modest effects on power.

C.8. Method and analyses related to Aim 2: Examine adoption characteristics that explain variability in implementation success. Remarkable variability in implementation success (i.e., reach, fidelity) has been documented among CBOs delivering evidence-based interventions.[125, 256] Similarly, it is expected that variation in characteristics of specific communities will be related to implementation of KIU! in this trial. We hypothesize that variability will exist among CBOs delivering KIU! and in the DTC arm. We will seek to explain the source of this variation with factors identified by CFIR[31]—a determinants framework commonly used to guide evaluation of factors that facilitate or hinder implementation of new interventions. We will evaluate factors from the 5 domains: **(1)** Outer setting factors include county characteristics (e.g., size, demographics), network links to other local organizations, and policies and incentives; **(2)** Inner setting factors include implementation support from CBO leadership, implementation climate, and implementation culture; **(3)** Characteristics of users (YMSM) include demographics and acceptability of KIU!; **(4)** Characteristics of the intervention include local adaptations, staff perceptions of quality and relative advantage over alternatives; and **(5)** process characteristics. Data on CFIR characteristics will be collected at the following data collection waves: prior to the launch of the application at each CBO site, immediately after launch, and then 4, 12, and 24 months following launch. Not all factors will be assessed at each wave of data collection—they are selected based on the phase of implementation.[257] The assessment schedule, measure being used, and respondents are specified in Table 2. Both CBO and DTC stakeholders (leaders, providers, staff) and YMSM in the program will participate. Given that some characteristics are only applicable to the CBOs, Table 2 also indicates those variables that are shared across the two arms and allow for direct comparison. Consistent with most implementation research projects, validated scales will be adapted and new scales created, as required.[258] As in our prior studies,[138-140, 186, 259-265] interview data will be transcribed and we will apply a thematic analysis approach to coding in Dedoose[262, 266] in which key conceptual domains are derived from existing literature[267, 268] and emerge from the data.[269, 270] Analyses will include qualitative and quantitative description and correlations with implementation outcomes described in aim 1.[262, 271]

Table 2. Aim 2 measurement. Note: * designates measures to be developed for this study. Wave 0 is launching of KIU.

	Construct	Administration	Respondent(s)	Arms	Wave
Inner	Implementation leadership[272] support	Survey, Interview	CBO and DTC Leaders & Staff	CBO	0-4
	Implementation climate and culture[273]	Survey, Interview	CBO and DTC Leaders & Staff	CBO	1,3
	Relative advantage of KIU! [274]	Survey, Interview	CBO and DTC Leaders & Staff	CBO	3,4
Outer	County characteristics	Survey, Interview	CBO and DTC Leaders & Staff, YMSM	CBO, DTC	0,2
	Policies and incentives*	Survey, Interview	CBO and DTC Leaders & Staff	CBO	3
	Participant needs and characteristics*	Survey	CBO and DTC Leaders & Staff, YMSM	CBO, DTC	0
KIU!	Knowledge of KIU!*	Survey	CBO and DTC Leaders & Staff, YMSM	CBO, DTC	2,4
	Acceptability of KIU!	KIU! usage data, Interview	CBO and DTC Leaders & Staff, YMSM	CBO, DTC	2,4
	KIU! Adaptability*	Survey, Interview	CBO and DTC Leaders & Staff	CBO	3
	Design quality and packaging of KIU!*	Survey	CBO and DTC Leaders & Staff, YMSM	CBO, DTC	2

C.9. Method and analyses to explore maintenance/sustainment of KIU! at the completion of the study. As an exploratory activity, we will evaluate the potential for institutionalization of KIU! in the CBOs after 2 years of implementation. CBOs will be provided with materials that they can use to apply for funding from their health department or other funders to continue to implement KIU! after the study is completed, including: (1) a report on their site-level implementation outcomes (e.g., number of YMSM reached, effectiveness at reducing HIV risk); (2) a budget Impact Tool that will allow each CBO to calculate the monetary impact during the study period and to estimate the cost for continued delivery of KIU! (created by our team's economists[32]). We will draw from our Sustainability Measurement System[33, 100] to examine the factors that predict applying for funding and sustaining use. We will also explore sustainment of the DTC arm by compiling the implementation outcomes for this strategy (e.g., estimated cost per infection averted) and report it to a group of strategic implementation advisors, including the CDC Division of HIV Prevention; the Third Coast CFAR Community

Advisory Board, and health departments. Consultant Levine has been a pioneer in the implementation of eHealth interventions in this area and will provide critical connections to Health 2.0 businesses. We will consult with the Northwestern Innovation and New Ventures Office (INVO), which supports Northwestern faculty moving innovations into the marketplace.

C.10. Summary. The goal of this application is to inform the scale up of eHealth HIV prevention programs. This is a timely and significant issue, as NIH has invested heavily in the development and testing of such programs, but the route forward to implementation is largely undefined. We propose to study the implementation of KIU! because it has established evidence of effectiveness on both behavioral and biomedical outcomes, as well as evidence of success in community-based implementations. Importantly, KIU! was developed and proven effective with diverse YMSM—the leading edge of the domestic HIV epidemic. As such, KIU! is an ideal intervention to study implementation and lessons learned in this trial will go beyond how to implement KIU! to inform implementation of other eHealth HIV interventions in the pipeline. We propose a rigorous **quasi-experimental** trial that will provide strong evidence for the head-to-head comparison of two pragmatic implementation strategies. Our trial has equipoise—either strategy could work better than the other (Aim 1) or work better in particular settings (Aim 2). Our proposal is highly ambitious—delivering KIU! in 22 US counties (CBO arm) and nationwide (DTC arm)—but our team's experience leading large scale studies, eHealth research, and quasi-experimental trials demonstrates our capacity to achieve our aims.

D. PROTECTION OF HUMAN SUBJECTS

As a behavioral HIV prevention trial, our study will be registered in Clinicaltrial.gov.

D.1. RISKS TO HUMAN SUBJECTS

D.1.a. Human Subjects Involvement, Characteristics, and Design

The primary participants will be racially and ethnically diverse young men who have sex with men (YMSM) aged 18–34, consistent with our previous KIU efficacy trial[13] and with findings regarding this age group as being at heightened risk for HIV and other STIs.[275-277] The investigative team has extensive experience conducting research with YMSM and will recruit participants under the oversight of Northwestern University's human subjects protection program. The Principal Investigator has been a member of the Institutional Review Board (IRB) and has expertise in ethical issues related to conducting research with sexual minority youth.[278, 279] The community-based organization (CBO) strategy arm will additionally involve stakeholders (leaders, provider, staff) from participating CBOs. The investigative team also has a history of successfully collaborating and conducting research with CBOs.

The project will begin with our refreshing the technology platform used in the previous KIU! trial to one that allows the program to be scalable to both implementation strategies, adaptable to local contexts, and updatable as new technologies and HIV-prevention options become available. During this deployment phase, 5-7 CBO staff and 10-12 diverse YMSM will be beta-testers of the near-to-final delivery system. The next phase comprises a type III hybrid implementation–effectiveness trial comparing the CBO strategy to the direct-to-consumer (DTC) approach among YMSM across the U.S. We will regularly consult the standing Youth Advisory Council of the Northwestern Institute for Sexual and Gender Minority Health and Wellbeing and the Third Coast Center for AIDS Research Community Collaboration Board on all aspects of the project, but these individuals are advisors rather than research participants so are not included here in our descriptions of human subjects issues.

In Phase 1 (year 1), the Technology Team will lead the necessary technological upgrades to the KIU! platform, based on our previous interviews with CBOs and the technical and logistical needs of both delivery strategies in the trial. Because Cook County will not be eligible to participate in the trial given the long history of KIU! delivery, 5-7 CBO staff and 10-12 diverse YMSM from Chicago will participate in usability and acceptability testing of the updated platform. A testing protocol established by the Northwestern Center for Behavioral Intervention Technologies (CBITs) will be used to assess usability across devices (e.g., computer, tablet, smartphone) and standards (e.g., bandwidths) and in practice with target participants who will "think out loud" as they go through the front-facing intervention and/or backend dashboard. Research staff will observe and take notes on participants' ability to navigate the technology. Participants will also be asked to respond to questions about the usability of the platform.

Test subjects for the Usability/Acceptability Testing will be selected from the IMPACT Program Research Participant database (STU00066112) who have previously consented to be contacted by providing basic demographic and e-mail or phone contact information at a variety of recruitment events, or who have completed the screener online by visiting the IMPACT program's website to sign up for possible future research studies. Subjects selected from the participant database will meet the basic inclusion criteria of the Phase 2 portion of the study: 1. Assigned Male at Birth (biological male), 2. Identify as gay or bisexual, or who report a history of sexual activity with other biological males, and 3. Ages 18 to 29 years old. A research assistant will follow the usability/acceptability recruitment script (see recruitment materials in eIRB+).

In Phase 2 (years 2-4), the RCT will enroll racially/ethnically diverse YMSM across the U.S. From the county-level sampling frame described in the research design, a stratified random sample of 75 counties will be selected and randomized 2:1 to the CBO and DTC strategies, respectively. In the DTC arm, Northwestern DTC team staff will directly recruit and deliver KIU! to YMSM in those counties. As of January 2021, the KIU! DTC strategy will not be limited to these randomized counties. The KIU! DTC strategy will expand to a nationwide catchment area. In the CBO arm, 50 counties will be eligible for CBOs to apply to implement KIU!, and we will ultimately select 25 CBOs (1 per county). Only 22 counties were actually randomized in the CBO arm due to grant budget cuts. Participating CBOs will integrate recruitment, delivery of KIU!, and study retention into their

routine HIV testing programs, with training and technical assistance from project staff at Northwestern. Given that most CBOs lack the technical capacity to host a complex eHealth application in-house, the KIU technology platform will continue to be supported by CBITs and staff at Northwestern. Because our study is a hybrid implementation trial, with reach to YMSM being one of the primary outcomes, the sample size of YMSM will not be set *a priori*.

In the CBO strategy arm, participants will have already received HIV testing and counseling from the participating CBOs as a condition for eligibility, using the same procedures as in the KIU efficacy trial. In the DTC arm, at-home HIV testing kits will be sent to potential participants eligible for the research components of the study. In both arms of the trial, we will test for Gonorrhea (NG) and Chlamydia (CT). In the DTC arm, we will use the commercially licensed Aptima STI sample collection kits with testing performed at the Marquette University Clinical Microbiology lab and use MTL BD ProbeTec Chlamydia trachomatis/Neisseria gonorrhoeae (CT/GC) Qx specimen collection kits with testing performing by MTL. We will refer for treatment as necessary at baseline and post-intervention. In the CBO arm, CBOs will perform the STI testing. Hologic, Inc., will provide training and technical assistance on implementing rectal STI testing as needed. For cases in which CBO-based STI testing is unavailable to participants, those participants will be shipped the Collection Kit.

All YMSM will receive the highly-interactive and YMSM-tailored Keep It Up! (KIU!) intervention. Consistent with meta-analytic data on effective HIV interventions, the content will be delivered over three sessions across a three-week period (see Appendix 1 for intervention overview), with two booster sessions at 6 and 12 weeks after competition of the intervention. The booster sessions continue to provide HIV-prevention motivation and behavioral-skills training.

YMSM participants in both conditions who are eligible for the research component of the study will complete all assessment materials. Similar procedures and measures successfully used in the developmental R34 study and the R01 efficacy trial will be employed. Assessments will be completed via the Internet using an Internet-based Computer-Assisted Self Interview (CASI). Assessments will occur at baseline and 12 weeks post intervention. At each log-in to the intervention, we will ask about the physical setting where the participant is located. We will assess levels of privacy, distractions, and the type of location. At each assessment point participants will be asked if they have experienced any adverse events as a result of their participation in the program. Endorsement of adverse events will trigger an email alert to the principal investigator who will respond expeditiously. Participants will also be given a contact number to call if they need more immediate assistance in regards to the adverse situation. Note that in the pilot and efficacy trials, no participants reported adverse events during the study.

In the CBO strategy arm only, CBO stakeholders (i.e., leaders and staff who consent to participate) will complete assessments immediately following training, but prior to the launch of the application at each CBO site, and then 4, 12, and 24 months following launch. DTC stakeholders (i.e., leaders and staff who consent to participate) will also complete an assessment in the final year of the study grant. These assessments will be conducted through online surveys via REDCap, telephone or video conference interviews, and potentially in-person interviews. Guided by the Consolidated Framework for Implementation Research (CFIR) determinants framework[31, 280] these assessments will explore organizational factors that that may be related to variability in implementation across CBOs.

Study inclusion criteria. We will include YMSM participants in the research component of the study if they (1) were male assigned at birth and identify as male or gender non-conforming; (2) received an HIV-negative test result from a participating CBO or self-report an HIV negative or unknown status (in the CBO arm), from a shipped HIV self-test kit or self-report an HIV negative or unknown status (in the DTC arm), or provide a copy of HIV test results by personally uploading results to REDCap or authorizing a healthcare provider to share results with the study team; and (3) are 18–34 years old. YMSM will be excluded from the study if they (1) do not have an e-mail address that can be used to contact them for retention purposes; (2) unable to read English at a minimum 8th grade level; (3) refuse to provide consent to participation. In the CBO strategy arm, CBOs will be eligible if they (1) have experience recruiting YMSM for HIV testing and (2) have the necessary infrastructure and organizational capacity to conduct the study activities. Both 1 and 2 will be determine during the review of CBO applications from our request for proposals (RFP).

Validating the respondents. The issue of confirming the identity of the respondent is not unique to technology-based studies. Respondents can easily lie about their identity in mail surveys and telephone

surveys where a respondent's age and sex are not always discernable from one's voice. The methodologies we plan for participant verification are drawn from these types of methods and replicate widely used procedures that have resulted in the collection of influential data. Our multi-pronged strategy to reduce the likelihood of respondent deception is consistent with best practices. We will employ these strategies as appropriate in both arms, but they are most germane to the DTC strategy where participants will primarily be enrolled in the program through online- and app-based advertising.

Online recruitment activities will disguise the qualifying criteria so those interested will not know what the "right" answers are for the eligibility screener. Eligibility confirmation will not be provided immediately, so it is not possible for participants to repeatedly change their responses on the screener to become eligible. We will enact verification procedures established in our prior online research[12, 142] and described in the literature:[190-194, 281] (1) perform an IP-lookup to determine if the IP addresses match the general location specified by participants and to assure that the address is in the US; (2) check name, email, and IP address for duplication; (3) review time-to-complete logs; (4) cross-validate responses across data collection points (e.g., date of birth at screening, age at baseline survey); and (5) seek further verification of their identity directly from them (e.g., photo of ID) and review of public information (e.g., Facebook page) for those who are identified as suspicious based on above criteria. During eligibility screening, we will also use the LexisNexis InstantID Verification process to check pieces of information shared by participants (e.g., full name, phone number, mailing address) against public records and publicly-available data sources to verify participants' identity. Participants will be given information about this process within the screener and asked if they agree to allow us to share their information with LexisNexis for these purposes. All participants are allowed to opt out of this InstantID Verification process. Those who chose to opt out will be contacted by a study team member to verify their identity over the phone by asking them questions from the eligibility screener and comparing their responses to those they entered when they completed online eligibility screener. In addition, as of September 2021, participants who have provided information during registration and in the baseline survey used to confirm eligibility that cannot be verified through the procedures described above will be contacted by study staff and asked to confirm their identity and eligibility via phone or video call in order to receive at-home HIV/STI test kits and payment for completed study activities. The type of call (traditional phone vs. video) will depend on the level of suspicion about the participant account as well as the participant's ability to access video call technology. At the beginning of the video calls, study staff will notify the participant that we will take a screenshot of their video image for security purposes and our records. The screenshots will be saved to a study folder on the secure Feinberg School of Medicine shared drive. Study staff will be able to refer back to these screenshots to check if a person is trying to participate many times under different identities. If the participant requests that we not take a screenshot of their video image, we will honor their request and make a note of this in their REDCap record. Study staff will also use the phone or video chat as an opportunity to answer any questions participants may have about participation in Keep It Up. Based on our previous studies conducted by the PI, this process takes typically takes 5 minutes.

Compensation. Participants in usability testing will be reimbursed $75 for approximately 90 minutes of their time and for travel expenses. Because of the RCT's pragmatic focus, and to match reimbursements across arms, compensation for YMSM participants for research participation will be minimized. YMSM will be automatically entered into an e-raffle (e.g., to win a preloaded gift card) for the completion of each assessment: baseline and 12 weeks. This payment schedule does not require the collection of tax documents from the participants. Participants in the DTC arm who complete the first three sessions of the intervention will receive a $50 virtual gift card, $10 for completing the 6-week follow-up, and $20 for completing the 12-week follow-up. DTC participants and CBO participants who complete at-home STI testing at 12-week follow-up will receive $20. Participants in the DTC arm will also be entered into an e-raffle for various prizes that have been donated by vendors (e.g. store brand gift cards, adult toys, condoms and lube) when they complete the 6 week booster and 12 week booster. This strategy is based on those successfully used by CBO partners in previous KIU! implementations to keep their clients engaged in the intervention. CBOs will follow their established internal guidelines for providing participants with incentives for participating in prevention activities like KIU! CBO stakeholders (leaders and staff) in the CBO arm will not be individually compensated for the completion of assessments because it will be a requirement of their organization's participation in the grant, as outlined in the Request for Proposal process (see Recruitment below). DTC stakeholders (leaders and staff) will also not be

individually compensated for the completion of the assessments. As of August 2022, participants in the CBO arm will also receive $20 for completing the 12-week follow-up survey.

D.1.b. Sources of Research Materials

Consistent with the pragmatic focus of this implementation trial, self-report measures from YMSM will be kept to a minimum (~10 minutes). We have used all of the proposed measures with YMSM in previous studies, including the KIU efficacy trial R01. Whenever possible, we selected measures (1) designed for high-risk YMSM to maximize sensitivity, (2) previously tested with diverse populations to minimize cultural bias, and (3) equivalent to other studies in order to maximize comparability of findings. Assessments will be securely collected via the Internet using an Internet-based Computer-Assisted Self-Interview (CASI) and REDCap software. Only the PI and Project Coordinators will have access to individually identifiable data, and data will be collected and stored on secure servers maintained by Northwestern (see below).

Questionnaire measures will assess constructs such as: demographics (e.g., age, race/ethnicity, education, SES, gender identity, sexual orientation, anatomic sex at birth); HIV risk behavior; experiences with PrEP; HIV testing; and intervention acceptability, tolerability, and process (e.g., where intervention was completed, reasons for non-participation, whether they experienced any adverse events as a result of participation).

STIs in the DTC strategy arm will be tested for using the BD ProbeTec Chlamydia trachomatis/Neisseria gonorrhoeae (CT/GC) Qx specimen collection kit or Aptima STI Test Collection Kit, consistent with the KIU 2.0 trial that produced a >90% return rate.[13] The BD ProbeTec CT/GC Qx specimen collection kit is manufacture by Becton, Dickinson and Company and kits are tested using the BD ProbeTec CT/GC Qx Amplified DNA Assays which detects Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) to aid in the diagnosis of chlamydial and/or gonococcal urogenital disease. The sensitivity and specificity for CT are 93.7 and 97%, respectively, while for GC they are 97.7 and 98.8%. The Aptima STI Collection Kit is manufactured by Hologic and kits are tested using the APTIMA Combo 2® Assay, which detects Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) to aid in the diagnosis of chlamydial and/or gonococcal urogenital disease. For CT, Hologic reports sensitivity of 96.5% (94.5% – 98.0%), specificity of 98.7% (98.2% – 99.2%) and an overall accuracy of 98.31%. They also report a false positive rate of 3.5% (2.0% – 5.5%) and false negative rate of 1.3% (.8% – 1.8%). For analysis of NG, Hologic reports sensitivity of 96.5% (94.4% – 98.0%), specificity 99.4% (99.0% – 99.7%) and an overall accuracy of 98.89%. They also report a false positive rate of 3.5% (2.0 – 5.6) and false negative rate of 0.6% (.3%-1.0%). The Marquette Clinical Microbiology Laboratory has performed concordance studies and the respective inter-laboratory agreement for CT and NG is excellent. In the CBO strategy arm, STI testing will be performed by the CBOs per their local procedures, with training and technical assistance support from Hologic as needed. Because of the very large market share for the Aptima test we expect it will be the most commonly used test. For selected CBOs that do not have the capacity for STI testing, or for participants who decline to return to a CBO for STI testing, those participants will be shipped the Aptima STI Test Collection Kit as in the DTC arm.

Selected CBO and DTC staff will also be asked to complete quantitative and qualitative assessments at specific points during the trial. These measures will include staff demographics, surveys on effectiveness of technical assistance and training, normalization process for implementation, organizational readiness for change, leadership engagement, implementation climate, readiness for e-Health, and sustainability. Prior to implementation, selected CBO staff will be asked to participate in qualitative interviews covering CFIR characteristics, including relative advantage of the intervention, adaptability, external policies and incentives, networks and communications, implementation climate, tension for change, compatibility, relative priority, and leadership engagement. DTC staff will also be asked to participate in a qualitative interview covering these CFIR characteristics during the final year of the study grant. These interviews will be audio and video recorded for data collection purposes.

D.1.c. Potential Risks

For YMSM, potential risks consist of the recruitment and assessment process (e.g., potential coercion, discomfort or distress during the intervention or assessments), loss of privacy during participation, and breaches of confidentiality. It is possible that certain assessment items (e.g., sexual behavior) may cause discomfort for some participants, but our prior ethics research on this topic suggests this is very rare.[282, 283]. There is a possibility that a participants' privacy will be compromised during study participation if they

participate on a device that is accessible by others or in a public space. There is a small possibility that a participant's information could be intercepted while in transit over the Internet or that data could be hacked from our servers. Finally, a participant could test HIV/STI positive during the course of the study as a result of our encouragement to obtain HIV/STI tests. While the result would be unrelated to study participation, we feel it is ethically important to articulate a plan for what we will do if this occurs.

These potential risks are taken very seriously by the researchers, and steps to reduce these risks are described in detail below. The investigative team has a history of working with community advisory boards to minimize recruitment and assessment risks for research and has an excellent record of online data collection informational security. The PI will be responsible for all aspects of the project with respect to study design, data collection, and use of data. Participants will have access to 24-hour referral information described below as well as phone numbers for the study administrators (i.e., PIs and IRB).

Consistent with the pragmatic focus of this implementation trial, CBOs in the CBO strategy arm will implement KIU! in line with their regular practices of delivering HIV testing, and thus, we expect potential risks of implementation to be minimal. It is possible that the cost of KIU! implementation to a CBO may exceed the funding provided by this grant and they may draw from other resources (this will be captured in our cost analysis). For CBO and DTC stakeholders (leaders, staff) participating in surveys, potential risks mirror those of the YMSM participants in terms of discomfort from the assessment process, loss of privacy, and breaches of confidentiality. Additionally, should a CBO or DTC staff participant's responses become known to the staff member's supervisor, there could be professional consequences if their responses are deemed objectionable to their supervisor. KIU Project staff will never disclose the individual responses CBO and DTC staff participants provide to their employer or supervisor. Finally, if a CBO or DTC staff participant refuses to participate in the study, there may be unforeseen professional consequences. KIU Project staff will not disclose to employers or supervisors which of their staff have refused to participate in the study.

D.2. ADEQUACY OF PROTECTION AGAINST RISKS

D.2.a. Recruitment and Informed Consent

YMSM in the DTC strategy arm will primarily be recruited using paid social media and gay app advertising, but we will also draw from the expertise of our advisory groups on innovative methods of recruiting diverse YMSM. Recruitment material will direct individuals to a study webpage with information about the service project component and a brief registration form. The webpage will mention that the service project component (e.g. KIU! intervention content) is provided as part of a research project. Potential participants will be directed to sign up by completing the registration form. If they register, potential participants will be sent an automated email with a link that they must click to confirm their account and set up password information. Once their password has been created, participants will watch a Welcome Video that describes KIU! After participants have watched the Welcome Video, they will be presented with a link to the full online consent form. If they consent by clicking the 'I Agree' button at the bottom of the page, their consent will be recorded in our database. We are asking for a waiver of documentation of the consent to complete the eligibility screener given that it is an online screener. Once consent is given, participants complete the online baseline survey with embedded eligibility questions about demographics and HIV status and additional contact information. Information collected this way will be encrypted and securely transmitted to the Northwestern server. Participants will provide a mailing addresses where they can receive a shipped HIV self-testing kit. After completing the survey, participants will be directed to the intervention content. YMSM in the CBO strategy arm will be recruited using the same procedures as in the KIU! R01 efficacy trial. YMSM who test HIV-negative through the CBOs' routine testing services and outreach events, or self-report a negative or unknown HIV status will be recruited. Using an internet-capable device and the KIU! platform, CBO staff will provide potential participants with information about the study and ask if they are interested and willing to be registered in the KIU! platform. If potential participants agree to being registered, CBO staff will collect and enter their name and email address into the KIU! platform. We are asking for a waiver of documentation of the consent for CBO staff to complete registration of potential participants given that it is an online registration system.

During registration, participants will also be offered the option to provide additional information such as a phone number, social media contact information should they prefer a contact method other than phone and email, and social support (e.g. family member or friend) contact information in case we are unable to reach the participant. Once the information has been entered into the KIU! platform, the platform will automatically send

an email to the email address provided inviting the participant to login to the KIU! platform and create their password. Once their password has been created, participants will watch a Welcome Video. After participants have watched the Welcome Video, they will be presented with a link to the full online consent form and an online baseline survey which includes questions to assess eligibility. After completing the survey, participants will be directed to the intervention content. As above, information collected this way will be encrypted and securely transmitted to the Northwestern server. Platform log-ins assigned to CBO staff will prevent unauthorized access to the encrypted information. The coordinating team for the CBO arm will provide training and supporting to CBO staff to assure easy compliance with this recruitment procedure.

In both study arms, non-response to the initial KIU! platform e-mail will trigger the retention protocol that includes a combination of automated reminders from the KIU! software as well as follow-up from CBO/DTC staff. The only data collected prior to informed consent will be registration information (CBO arm) and screening data (DTC arm) used to assure eligibility and reasons for non-participation.

As stated in the research design, CBOs in counties randomized to the CBO strategy arm will be selected through a Request for Proposal (RFP) process. The RFP will be disseminated through state health department HIV programs and national HIV/AIDS organizations. It will describe the study, eligibility criteria, and activities to be conducted as part of the study, the latter of which includes staff participation in research activities (i.e., surveys and telephone interviews). As stated above, selected CBO and DTC staff members will be asked to participate in both quantitative and qualitative surveys and interviews. CBO staff will be identified by KIU project staff by asking primary contacts at each CBO for the contact information of staff members who qualify to participate. KIU project staff will then contact the individual CBO staff members directly. All DTC staff in the final year of the study grant will be asked to participate in the surveys and interviews. Selected CBO and DTC staff will be consented into the research aspects similar to YMSM participants of the trial.

Informed consent in Phase 1 usability testing, where YMSM and CBO participants come in person to the lab, will obtained in writing. In Phase 2, consent will be obtained online using procedures that have been used successfully, with IRB approval, in previous studies, including the KIU! developmental R34 and KIU! R01 efficacy trial (see Preliminary Studies). The consent document will be written to Federal OHRP standards with 8th grade or below reading level. The consent statements will have the required elements of informed consent, including (a) a description of the study and the amount of time required for participation; (b) acknowledgment that participation is voluntary and that no negative consequences will occur for those who choose not to participate; (c) acknowledgment of the participant's right to withdraw at any time; (d) guarantee of confidentiality unless any person is in danger of injury; (e) a statement of payment, including amount and circumstances under which the respondent would not be paid (including early withdrawal from the study); and (f) contact information for relevant investigators and IRB members. Participants will answer three questions at the end of the consent form to confirm their understanding of the study and their responsibilities as a participant. If the participant does not respond correctly to any of the questions, study staff will follow-up with a phone call to assess their understanding of the study requirements and address any questions or concerns.

D.2.b. Protection Against Potential Coercion

We will work with the IRB to assure compliance with ethical and HIPAA standards. Specifically, participants will provide all information, no personal health information will be provided by the testing staff, testing staff will not be given incentives for recruiting participants, and peer recruitment will not be incentivized. We will make it clear to participants that their decision regarding participation will not affect in any way potential future interactions with the university or their access to services. CBO leadership will not be provided incentives for recruiting or referring CBO staff for participation. Selected CBO staff will also not receive additional payment for participation.

D.2.c. Protection Against Discomfort

Multiple IRB-monitored studies at Northwestern University have used our proposed measures with no known adverse effects. Participants will be told that they do not have to answer any question they do not wish to. Participants will be instructed that they can take a break and return to the online assessments or modules at a later time if they are experiencing mild distress. In the unlikely event that a participant experiences considerable distress they will be instructed to contact the Tracking Coordinator, who can assist in making

appropriate local referrals or who will refer them, as appropriate, to the PI (who is a Licensed Clinical Psychologist).

D.2.d. Protection Against a Breach of Confidentiality
Publications will only use aggregated data. No report of individual data will be provided. The research team will have bi-weekly phone- or video- conferences to monitor the progress of the study. We will take several steps to prevent a breach of confidentiality.

Personal privacy. We will ask participants if we can cite the study in phone messages that we may leave. No supplemental contact information (e.g., additional phone number, friend's number, physical address) outside of that collected during registration will be required to enroll; participants will only provide the information if they choose to and can do so safely.

Protecting privacy during online data collection. The investigative team has conducted numerous online studies with very sensitive questions. There are many benefits to this methodology, including increased self-disclosure compared to interviewer-based data collection; convenience for the participant as he can decide when to complete it; and increased safety as he can decide when and where it is best to answer these questions. There are several things we do to ensure privacy: disable the back button so that no one can click back into the survey to see what the answers are; tell participants that they need to be in a private place – and then ask them follow up questions to see if they are (and if they are not, encourage them to come back to the survey later); and explain to participants how to clear their browser history.

Secure electronic transmissions and storage of data. We have developed systematic protocols for data handling and storage over longitudinal online studies. CBITs has multiple mechanisms for providing data security in the transfer of data from client machines to CBITs servers. These webservers use Secure Socket Layer (SSL or https) technology to encrypt data exchanged between the client and the server. SSL will be implemented in all systems built for the project to ensure the encryption of data during transmission from the participants' workstations to CBITs servers. All project data will be stored on secured, password-protected database servers behind passcode-protected doors. All components of the data system will be accessible only through a login and password unique to each assigned user on the study team. The security access levels for these login accounts will be tiered based on specific roles and responsibilities for the project. The features and privileges associated with each role and subsequent access level will be determined based on the level of access to confidential data needed by each team member. For example, only project staff who maintain personal contact with participants will be given access to personal identifying information. Tracking staff will not be given access to survey data, so they cannot link identifying information to participant data. All other team members will only have access to data that are tied to a random ID number and that cannot be used to personally identify the participant. Database administrators in CBITs who manage the technology will only access the database with names and contact information when absolutely necessary for maintaining the database. De-identified data will be stored indefinitely on secure shared drives housed on Northwestern's servers. (1) All study staff, including CBITs staff, will be trained in Human Subjects research and will sign confidentiality agreements prior to participation in the project. (2) All names and contact information for the follow-up of participants will be stored in a database that is separate from the participant's responses to the assessment. Only a random study ID will be stored with the participant's data for linkage to subsequent data later. (3) As we have done in over nearly a dozen prior studies, we will obtain a Certificate of Confidentiality issued by the federal government and the certificate will be maintained through the life of the research project. These certificates are now routinely granted to NIH-funded studies. This helps protects the data from subpoena and thus prevents the data from being used against the participant. (4) We will inform study participants of the limits of the certificate of confidentiality during the consent process.

To help protect participants' confidentiality while they complete the Internet-based assessments and intervention modules, we will: (1) remind participants each time they log on that they will be answering personal questions; (2) encourage them to complete the modules and questionnaires in a private environment; and (3) suggest spaces with greater privacy (e.g. in their dorm room with the door closed, at a coffee shop in an area where no one can look over their shoulder). All project staff (from investigators to research associates) have extensive experience interacting with our research populations in a sensitive and understanding manner

so as to increase the comfort of research participants and ensure comprehensive and valid data collection. In addition, all have completed the required on-line training for the protection of human subjects. Our use of self-administered electronic systems for collecting data will also serve to enhance the reliability and validity of the data from each participant. Private self-report increases the proportion of individuals admitting sexual behaviors and illicit drug use. As such, these measurement modalities allow for greater respondent privacy and remove barriers to honest responding, such as embarrassment, feedback from interviewer facial expressions, and other social influences. Given the online nature of this study, our CBITs team will include professional quality assurance staff who will provide software testing and troubleshooting for new and existing CBITs systems, including development of test plans, test cases and test scripts. The CBITs team will ensure that the intervention functionality operates properly and that the content is accurate, complete and clear.

We have also developed procedures with the STI testing laboratories, Marquette University Clinical Microbiology Lab and Molecular Testing Labs, to prevent a breach of confidentiality. (1) The labs will shred any shipping material that contain identifiable information (e.g., return address). (2) Internal material within the shipping box does not contain identifiable information. Participants will be given unique user IDs and passwords for all STI testing materials and for accessing STI test results. (3) Electronic communications regarding test results between the Marquette lab and Northwestern will be conducted via email of a de-identified Excel spreadsheet. This spreadsheet will only identify participants by a unique subject ID number and not include any PHI or PII. (4) Electronic communications regarding test results between MTL and Northwestern will be conducted via the secure MTL web portal.

D.2.e. HIV Seroconversion and STI Diagnosis During the Course of the Study

Participation in KIU! begins after receiving a negative HIV test result or self-report of an HIV negative or unknown status. For participants who complete at-home testing using MTL specimen collection kits, fingersticks may cause temporary discomfort and rarely, infection. Some persons may pass out at the sight of blood, but this is rare. Some participants may test HIV positive at CBOs or in at home test kits that we ship to them. We will utilize procedures we have developed across studies involving at home HIV testing of over 3,000 MSM (e.g., KIU! 2.0, Know@Home, One Thousand Strong) we will make referrals into HIV care for anyone who receives a positive HIV test. We have access to several databases (e.g., AIDSVu led by Consultant Patrick Sullivan) that we can draw from to identify local HIV care services for participants in the DTC arm. We have also added resources (e.g. the website telehealth.hhs.gov) that identify telehealth HIV care services that participants can use during the COVID-19 pandemic stay-at-home orders. After initial enrollment and intervention completion, if a participant reports an HIV seroconversion on the questionnaires, he will still be eligible to participate in subsequent assessments. Participants who report seroconversion during the study will be appropriately referred for care at the CBO that recruited them (in the CBO arm), at a clinic in their local area (in the DTC arm), or elsewhere based on their requests. We will maintain lists of referrals and will assist in making linkages to care.

Participants will be tested for Gonorrhea and Chlamydia at baseline and post-intervention. To receive their STI test results, participants call or visit a secure website using their unique ID and password. Participants may speak to a staff member or a laboratory technician if they have any questions or concerns about their results. For those who are positive for Chlamydia or Gonorrhea, we are legally required to report the results to state or local health department and we will also following-up with the participants to be sure they receive appropriate medical attention. We provide a cover letter to the lab report explaining that the participant was tested in the context of a research study, which participants can take to a provider to obtain treatment. The ability to link YMSM to needed clinical services is a distinct strength of this proposal as the multi-disciplinary investigative has considerable experience doing research with high-risk youth populations, and the program of research is embedded in a larger network of CBOs designed to meet the needs of YMSM.

D.3. POTENTIAL BENEFITS OF THE STUDY TO THE SUBJECTS AND OTHERS

There are several potential benefits to this study. YMSM may benefit by reducing their risky sexual behavior, accessing HIV testing and other risk reduction services, and decreasing their risk of HIV/STI infection as a result of participation in KIU!. CBOs may benefit from the collected evaluation data by improving existing HIV testing services and delivering prevention programs to YMSM. CBO staff who participate may benefit through feeling good about contributing to scholarship and providing and innovative service to their clients. Society will benefit from expanding scholarship on e-health implementation at community-based and other social service

settings as well as the scaling out of an effective eHealth intervention that reduces risk behavior and STI incidence among YMSM, limiting the spread of HIV, and addressing health disparities. Possible risks are outweighed by this potential to reduce HIV/STI-risk among YMSM.

D.4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Rising HIV infection rates among YMSM and a lack of knowledge on how to scale out eHealth evidence-based prevention programs warrants research on the dissemination and implementation of an online HIV-prevention program tailored for this population. The purpose of this study is to systematically compare two pragmatic implementation strategies of our highly engaging and effective KIU! program. Currently, substantial investment from the NIH is being put into the development and testing of eHealth HIV interventions for efficacy, but the impact of those programs in real-world settings will be dependent on effective implementation (i.e., ensuring effective interventions reach the right individuals at the right time in the right dose). Our study represents an opportunity to identify and understand effective implementation approaches of eHealth HIV-prevention programs to ensure that the promise of cost-effective scalability is realized.

D.5. DATA SAFETY AND MONITORING PLAN

D.5.a. Procedures for Monitoring Data Management and Integrity

To protect the integrity of the participant's data, the system will assign each individual a unique random ID number at study enrollment. Access to identifying information will be limited to staff who play a direct role in the recruitment and retention of participants and we will limit their access to participant self-report data. All personnel will complete extensive training before they are granted access to identifying information. They will complete Human Subjects training at Northwestern University or other performance sites, which complies with federal guidelines delineated in 45 CFR Part 46. Personnel sign confidentiality statements that specify that if the participant's confidentiality is breached unintentionally, personnel will follow the procedures for reporting this breach to the Principal Investigator. The confidentiality statement also states that unintentional or deliberate violations of participant's confidentiality may result in termination depending upon the severity of the event. Personnel will also participate in training regarding data safety, confidentiality of participants, limits of confidentiality, and proper administration of the study protocol. We will store all data in databases that will be maintained on password-protected and fire-walled servers, maintained by Northwestern. Access to the system interface will require a separate password. Only the PI and the study coordinators will have access to this subdirectory. The PI will review all requests, current and future, to use the data. Any data files that are provided to other individuals will be stripped of identifiers other than random ID numbers.

D.5.b. Procedures for Monitoring Adverse Events

All study personnel, particularly the study coordinators, will be trained regarding how to handle adverse events. Possible adverse events that are unanticipated will be brought to the attention of the Principal Investigator and reported immediately to the Northwestern University and other engaged institutions (as required). The IRBs will determine whether it is appropriate to stop the study protocol temporarily or will provide suggestions/modifications to the study procedures as necessary. Possible modifications include adding these possible adverse events to the consent forms and re-consenting all study participants. The PI will be responsible for monitoring participant safety on a monthly basis at regularly scheduled research meetings. He will keep a log of all events and ensure that the IRB is contacted immediately. He will also keep a log of the outcome of IRB decisions regarding adverse events and apprise the research team of any changes that need to occur as a result of IRB decisions.

Given the online nature of the study, special procedures are required to identify adverse events. To identify adverse events we will: (1) instruct participants to report any adverse events to the research team as soon as possible via e-mail or phone. Such a report will immediately be brought to the attention of the PI. (2) At each assessment, we will ask participants if they have experienced any adverse events. Their responses to these items will be programmed to be e-mailed to the research team upon submission, who will then immediately forward them to the PI.

D.5.c. Data Safety and Monitoring Board

In accordance with the National Institutes' of Health requirement that clinical trials have Data and Safety Monitoring Boards (DSMB), we will establish a DSMB according to policies and requirements put forth by NIH.

Dr. Mustanski, the application PI, has served on numerous DSMBs for HIV prevention trials and is familiar with their organization and operation. The proposed study is considered to present minimal risk to participants given that subjects will complete questionnaires, receive STI tests, and participate in a behavioral intervention.

The Northwestern University Clinical and Translational Sciences Institute (NUCATS) will assist in establishing protocols for managing the DSMB. The DSMB will be comprised of at least 3 members external to Northwestern. Across members, there will be expertise in eHealth, HIV prevention with MSM, and clinical trial methodology. Member will be nominated by the PI and approved by the NIH program officer. All DSMB members will be voting members and will be appointed for the life of the project, unless a conflict of interest arises.

DSMB member responsibilities. Members of the DSMB will perform the following activities: (a) Review the research protocol and plans for data and safety monitoring. (b) Review progress of the trial, including analysis of data quality and timeliness; subject recruitment, randomization and retention; subject risk versus benefit; and other factors that may affect outcome. (c) Review serious adverse event reports, provide commentary, and provide oversight to ensure that reports are relayed to individual IRBs and to the Office of Human Research Protections (OHRP), as indicated. (d) Review analyses of outcome data of the proposed study and review reports of related studies. (e) Determine whether the trial should continue as designed, should be changed, or should be terminated based on the data and make recommendations to the NIH, Institutional Review Boards, and investigators considering conclusion or continuation of the study. (f) Review significant modifications to the study prior to their implementation. (g) Protect the confidentiality of the trial data and the results of the monitoring. (h) Determine whether and to whom outcome results should be released prior to the reporting of study results. (i) Following DSMB meetings, provide appropriate NIH staff and the PI with written information concerning their findings.

DSMB meetings. DSMB meetings will be held every twelve months beginning in Year 2 of the study. However, the Chair of the DSMB can call a meeting as needed. Serious adverse events will be reported to the Chair as soon as they occur. The Chair of the DSMB will determine whether a teleconference is needed. Prior to the meetings, a written report containing any outcome data will be sent to DSMB members by the study statistician. Each meeting will be divided into three parts. (1) There will be an open session in which the PI will be present to review the progress of the study and to answer questions from members of the DSMB. (2) A closed session involving the DSMB members and the study statistician will be held during which outcome results will be discussed. (3) A final session involving only the DSMB members will be held to discuss the progress of the study and the outcome results, to develop recommendations, and to takes votes as necessary.

DSMB recommendations. The DSMB recommendations will be given to the PI. If the DSMB recommends a change to the study or that a study be closed, the PI will act as quickly as possible upon those recommendations. If the PI disagrees with the DSMB, the NIH Project Officer will be notified and all parties will reach a mutually acceptable decision. Confidentiality will be maintained throughout this process unless relevant data need to be presented in order to reach a mutually acceptable decision.

Release of outcome data. Outcome data will not be made available to individuals outside of the DSMB. Each member of the DSMB will sign a statement of confidentiality.

Conflict of interest. Members of the DSMB will disclose any potential conflicts of interest, either preexisting or those that develop during their tenure, to the PI and the NIH Project Officer.

REFERENCES

1. Allison S, Bauermeister JA, Bull S, Lightfoot M, Mustanski B, Shegog R, Levine D. The intersection of youth, technology, and new media with sexual health: moving the research agenda forward. *J Adolesc Health*. 2012;51:207-12; PMCID: PMC4330086.
2. Hightow-Weidman LB, Muessig KE, Bauermeister J, Zhang C, LeGrand S. Youth, Technology, and HIV: Recent Advances and Future Directions. *Curr HIV/AIDS Rep*. 2015;12:500-15; PMCID: PMC4643403.
3. Muessig KE, Nekkanti M, Bauermeister J, Bull S, Hightow-Weidman LB. A systematic review of recent smartphone, Internet and Web 2.0 interventions to address the HIV continuum of care. *Curr HIV/AIDS Rep*. 2015;12:173-90; PMCID: 4370788.
4. Noar SM, Willoughby JF. eHealth interventions for HIV prevention. *AIDS Care*. 2012;24:945-52; PMCID: PMC4529749.
5. Cao B, Gupta S, Wang J, Hightow-Weidman LB, Muessig KE, Tang W, Pan S, Pendse R, Tucker JD. Social Media Interventions to Promote HIV Testing, Linkage, Adherence, and Retention: Systematic Review and Meta-Analysis. *J Med Internet Res*. 2017;19:e394; PMCID: PMC5722976.
6. Noar SM, Pierce LB, Black HG. Can Computer-Mediated Interventions Change Theoretical Mediators of Safer Sex? A Meta-Analysis. *Human Communication Research*. 2010;36:261-97.
7. Bailey JV, Murray E, Rait G, Mercer CH, Morris RW, Peacock R, Cassell J, Nazareth I. Interactive computer-based interventions for sexual health promotion. *Cochrane Database Syst Rev*. 2010:CD006483.
8. Bailey J, Mann S, Wayal S, Hunter R, Free C, Abraham C, Murray E. Sexual health promotion for young people delivered via digital media: A scoping review. *Public Health Research*. 2015;3.
9. Mohr DC, Lyon AR, Lattie EG, Reddy M, Schueller SM. Accelerating Digital Mental Health Research From Early Design and Creation to Successful Implementation and Sustainment. *J Med Internet Res*. 2017;19:e153; PMCID: PMC5443926.
10. Mohr DC, Weingardt KR, Reddy M, Schueller SM. Three Problems With Current Digital Mental Health Research . . . and Three Things We Can Do About Them. *Psychiatr Serv*. 2017;68:427-9.
11. Greene GJ, Madkins K, Andrews K, Dispenza J, Mustanski B. Implementation and Evaluation of the Keep It Up! Online HIV Prevention Intervention in a Community-Based Setting. *AIDS Educ Prev*. 2016;28:231-45.
12. Mustanski B, Garofalo R, Monahan C, Gratzer B, Andrews R. Feasibility, acceptability, and preliminary efficacy of an online HIV prevention program for diverse young men who have sex with men: the Keep It Up! intervention. *AIDS Behav*. 2013;17:2999-3012; PMCID: PMC3796205.
13. Mustanski B, Madkins K, Greene GJ, Parsons JT, Johnson BA, Sullivan P, Bass M, Abel R. Internet-based HIV prevention with at-home sexually transmitted infection testing for young men having sex with men: study protocol of a randomized controlled trial of Keep It Up! 2.0. *JMIR Res Protoc*. 2017;6:e1; PMCID: PMC5251167.
14. Mustanski B, Parsons JT, Sullivan P, Madkins K, Rosenberg E, Swann G. A randomized controlled trial of the Keep It Up 2.0 eHealth HIV prevention program on biomedical and behavioral outcomes. *Manuscript under review*. 2017.
15. Brown CH, Curran G, Palinkas LA, Aarons GA, Wells KB, Jones L, Collins LM, Duan N, Mittman BS, Wallace A, Tabak RG, Ducharme L, Chambers DA, Neta G, Wiley T, Landsverk J, Cheung K, Cruden G. An Overview of Research and Evaluation Designs for Dissemination and Implementation. *Annual Review of Public Health, Vol 38*. 2017;38:1-22.
16. Grey JA, Bernstein KT, Sullivan PS, Purcell DW, Chesson HW, Gift TL, Rosenberg ES. Estimating the Population Sizes of Men Who Have Sex With Men in US States and Counties Using Data From the American Community Survey. *JMIR Public Health Surveill*. 2016;2:e14; PMCID: PMC4873305.
17. Gustafson DH, Brennan PF, Hawkins R. Investing in e-health: What it takes to sustain consumer health informatics. New York: Springer; 2007. x, 234 p. p.
18. Harris CM, Burns J, Gregorich T, Kall G, Piar PM, Miller HD, Schaffer JL. Managing technology in a complex healthcare delivery system. *J Healthc Inf Manag*. 2003;17:37-41.

19. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Med Care*. 2012;50:217-26; PMCID: PMC3731143.
20. Abrams DB, Orleans CT, Niaura RS, Goldstein MG, Prochaska JO, Velicer W. Integrating individual and public health perspectives for treatment of tobacco dependence under managed health care: a combined stepped-care and matching model. *Ann Behav Med*. 1996;18:290-304.
21. Glasgow RE, Klesges LM, Dzewaltowski DA, Estabrooks PA, Vogt TM. Evaluating the impact of health promotion programs: using the RE-AIM framework to form summary measures for decision making involving complex issues. *Health Educ Res*. 2006;21:688-94.
22. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health*. 1999;89:1322-7; PMCID: PMC1508772.
23. CDC Division of HIV/AIDS Prevention. Turning the Tide on HIV: Division of HIV/AIDS Prevention Annual Report 2013. Atlanta, GA: Centers for Disease Control and Prevention, 2013.
24. Purcell D. CDC's approach to high-impact HIV prevention in the era of expanding prevention options. 23rd Annual Illinois State HIV/STD Conference; Springfield, IL2014.
25. Proctor E, Silmere H, Raghavan R, Hovmand P, Aarons G, Bunger A, Griffey R, Hensley M. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Adm Policy Ment Health*. 2011;38:65-76; PMCID: PMC3068522.
26. Bell SG, Newcomer SF, Bachrach C, Borawski E, Jemmott JB, 3rd, Morrison D, Stanton B, Tortolero S, Zimmerman R. Challenges in replicating interventions. *J Adolesc Health*. 2007;40:514-20; PMCID: PMC1976555.
27. Neumann MS, Sogolow ED. Replicating effective programs: HIV/AIDS prevention technology transfer. *AIDS Educ Prev*. 2000;12:35-48.
28. Kegeles SM, Rebchook G, Tebbetts S, Arnold E, Team T. Facilitators and barriers to effective scale-up of an evidence-based multilevel HIV prevention intervention. *Implement Sci*. 2015;10:50; PMCID: PMC4405833.
29. Aarons GA, Fettes DL, Sommerfeld DH, Palinkas LA. Mixed methods for implementation research: application to evidence-based practice implementation and staff turnover in community-based organizations providing child welfare services. *Child Maltreat*. 2012;17:67-79; PMCID: PMC3841106.
30. Palinkas LA, Roades Cooper B. Mixed methods evaluation in dissemination and implementation science. In: Brownson RC, Colditz GA, Proctor EK, editors. Dissemination and implementation research in health. 2nd ed. New York, NY: Oxford University Press; 2017.
31. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4:50; PMCID: PMC2736161.
32. Center for Health Economics of Treatment Interventions for Substance Use Disorders H, and HIV (CHERISH). Budget Impact Tool New York, NY: Weill Cornell Medicine, Boston Medical Center, University of Pennsylvania, and University of Miami; 2015 [9 January 2018]. Available from: http://cherishresearch.org/resources/#BudgetImpact.
33. Palinkas LA, Spear SE, Mendon SJ, Villamar J, Valente T, Chou CP, Landsverk J, Kellam SG, Brown CH. Measuring sustainment of prevention programs and initiatives: a study protocol. *Implement Sci*. 2016;11:95; PMCID: PMC4947241.
34. CDC. HIV surveillance in adolescents and young adults. 2013.
35. CDC. HIV Infection Risk, Prevention, and Testing Behaviors among Men Who Have Sex with Men - National HIV Behavioral Surveillance, 20 U.S. Cities, 2014. 2016.
36. CDC. Diagnoses of HIV Infection among Adolescents and Young Adults in the United States and 6 Dependent Areas 2010-2014 Atlanta, GA: Centers for Disease Control and Prevention; 2016 [26 March 2017]. Available from: http://www.cdc.gov/hiv/library/reports/surveillance/.
37. Beck EC, Birkett M, Armbruster B, Mustanski B. A data-driven simulation of HIV spread among young men who have sex with men: role of age and race mixing and STIs. *J Acquir Immune Defic Syndr*. 2015;70:186-94; PMCID: PMC4573360.

38. Crepaz N, Marks G, Mansergh G, Murphy S, Miller LC, Appleby PR. Age-related risk for HIV infection in men who have sex with men: examination of behavioral, relationship, and serostatus variables. *AIDS Educ Prev*. 2000;12:405-15.
39. Garofalo R, Hotton AL, Kuhns LM, Gratzer B, Mustanski B. Incidence of HIV infection and sexually transmitted infections and related risk factors among very young men who have sex with men. *J Acquir Immune Defic Syndr*. 2016;72:79-86; PMCID: PMC Journal in Process.
40. Halkitis P, Kapadia F, Ompad D. Incidence of HIV infection in young gay, bisexual, and other YMSM: The P18 cohort study. *J Acquir Immune Defic Syndr*. 2015;69:466-73; PMCID: PMC4484878.
41. CDC. HIV Surveillance Report, 2016. 2017 November 2017. Report No.
42. Sullivan PS, Peterson J, Rosenberg ES, Kelley CF, Cooper H, Vaughan A, Salazar LF, Frew P, Wingood G, Diclemente R, del Rio C, Mulligan M, Sanchez TH. Understanding racial HIV/STI disparities in black and white men who have sex with men: a multilevel approach. *PLoS ONE*. 2014;9:e90514; PMCID: 3946498.
43. Steele BC, Melendez-Morales L, Campoluci R, DeLuca N, Dean HD. Health disparities in HIV/AIDS, viral hepatitis, sexually transmitted dieseases, and Turberculosis: Issues, burden, and response, a retrospective review 2000-2004. Atlanta: Center for Disease Control and Prevention, 2007.
44. CDC. Sexually transmitted disease surveillance 2015. Atlanta: US Deptartment of Health and Human Services, 2016.
45. Kelley CF, Vaughan AS, Luisi N, Sanchez TH, Salazar LF, Frew PM, Cooper HL, Diclemente R, del Rio C, Sullivan PS, Rosenberg ES. The effect of high rates of bacterial sexually transmitted infections on HIV incidence in a cohort of black and white men who have sex with men in Atlanta, Georgia. *AIDS Res Hum Retroviruses*. 2015;31:587-92; PMCID: 4458736.
46. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhea and chlamydia reinfection is associated with increased risk of HIV seroconversion. *J Acquir Immune Defic Syndr*. 2010;53:537-43.
47. Barbee LA, Khosropour CM, Dombrowksi JC, Golden MR. New Human Immunodeficiency Virus diagnosis independently associated with rectal Gonorrhea and Chlamydia in men who have sex with men. *Sex Transm Dis*. 2017;44:385-9; PMCID: PMC5481158.
48. CDC. HIV risk and prevention estimates Atlanta, GA: Division of HIV/AIDS Prevention; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention; Centers for Disease Control and Prevention; 2017 [3 November 2017]. Available from: https://www.cdc.gov/hiv/risk/estimates/index.html.
49. Mustanski B, Feinstein BA, Madkins K, Sullivan P, Swann G. Prevalence and Risk Factors for Rectal and Urethral Sexually Transmitted Infections From Self-Collected Samples Among Young Men Who Have Sex With Men Participating in the Keep It Up! 2.0 Randomized Controlled Trial. *Sex Transm Dis*. 2017;44:483-8.
50. CDC. Compendium of evidence-based interventions and best practices for HIV prevention 2017 [updated April 7, 2017; cited 2017 June 26]. Available from: https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html.
51. Mustanski B, Fisher CB. HIV rates are increasing in gay/bisexual teens: IRB barriers to research must be resolved to bend the curve. *Am J Prev Med*. 2016;51:249-52; PMCID: PMC4958583.
52. Shoptaw S, Weiss RE, Munjas B, Hucks-Ortiz C, Young SD, Larkins S, Victorianne GD, Gorbach PM. Homonegativity, Substance Use, Sexual Risk Behaviors, and HIV Status in Poor and Ethnic Men Who Have Sex with Men in Los Angeles. *Journal of Urban Health : Bulletin of the New York Academy of Medicine*. 2009;86:77-92.
53. Mustanski B, Newcomb M, Du Bois SN, Garcia SC, Grov C. HIV in young men who have sex with men: A review of epidemiology, risk and protective factors, and interventions. *J Sex Res*. 2011;48:218-53; PMCID: PMC3351087.
54. Arnett JJ. Conceptions of the transition to adulthood: Perspectives from adolescence through midlfe. *Journal of Adult Development*. 2001;8:133-43.
55. Arnett JJ. Conceptions of the transition to adulthood among emerging adults in American ethnic groups. *New Dir Child Adolesc Dev*. 2003:63-75.

56. Swendeman D, Rotheram-Borus MJ. Innovation in sexually transmitted disease and HIV prevention: internet and mobile phone delivery vehicles for global diffusion. *Curr Opin Psychiatry*. 2010;23:139-44; PMCID: PMC2881840.
57. Kelly JA, Spielberg F, McAuliffe TL. Defining, designing, implementing, and evaluating phase 4 HIV prevention effectiveness trials for vulnerable populations. *J Acquir Immune Defic Syndr*. 2008;47 Suppl 1:S28-33; PMCID: PMC2409151.
58. Rietmeijer CA. Risk reduction counselling for prevention of sexually transmitted infections: how it works and how to make it work. *Sex Transm Infect*. 2007;83:2-9; PMCID: PMC2598584.
59. Solomon J, Card JJ, Malow RM. Adapting efficacious interventions: Advancing translational research in HIV prevention. *Eval Health Prof*. 2006;29:162-94.
60. CDC. High-impact HIV prevention: CDC's approach to reducing HIV infections in the United States. Centers for Disease Control and Prevention; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention; Division of HIV/AIDS Prevention, 2011.
61. Kegeles SM, Hays RB, Coates TJ. The Mpowerment Project: A community-level HIV prevention intervention for young gay men. *Am J Public Health*. 1996;86:1129-36.
62. Jones KT, Gray P, Whiteside YO, Wang T, Bost D, Dunbar E, Foust E, Johnson WD. Evaluation of an HIV prevention intervention adapted for Black men who have sex with men. *Am J Public Health*. 2008;98:1043-50; PMCID: 2377294.
63. Glasgow RE, Eckstein ET, Elzarrad MK. Implementation science perspectives and opportunities for HIV/AIDS research: integrating science, practice, and policy. *J Acquir Immune Defic Syndr*. 2013;63 Suppl 1:S26-31.
64. McCray E. Envisioning a bolder agenda for implementation science to improve HIV prevention and care outcomes. National CFAR Scientific Symposium; Washington, DC2017.
65. National Institutes of Health Office of AIDS Research. NIH HIV/AIDS Research Priorities and Guidelines for Determining AIDS Funding Bethesda, MD2015 [13 August 2015]. Available from: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-137.html.
66. Oh H, Rizo C, Enkin M, Jadad A. What is eHealth (3): a systematic review of published definitions. *J Med Internet Res*. 2005;7:e1; PMCID: 1550636.
67. Lenhart A. Teen, Social Media and Technology Overview 2015. Pew Research Center, 2015.
68. Bowen AM, Horvath K, Williams ML. A randomized control trial of Internet-delivered HIV prevention targeting rural MSM. *Health Educ Res*. 2007;22:120-7; PMCID: 2639555.
69. Bowen AM, Williams ML, Daniel CM, Clayton S. Internet based HIV prevention research targeting rural MSM: feasibility, acceptability, and preliminary efficacy. *J Behav Med*. 2008;31:463-77; PMCID: 2614302.
70. Noar SM. Computer technology-based interventions in HIV prevention: state of the evidence and future directions for research. *AIDS Care*. 2011;23:525-33.
71. Guse K, Levine D, Martins S, Lira A, Gaarde J, Westmorland W, Gilliam M. Interventions using new digital media to improve adolescent sexual health: a systematic review. *J Adolesc Health*. 2012;51:535-43.
72. Hassan A, Scherer EA, Pikcilingis A, Krull E, McNickles L, Marmon G, Woods ER, Fleegler EW. Improving Social Determinants of Health: Effectiveness of a Web-Based Intervention. *Am J Prev Med*. 2015;49:822-31.
73. Bauermeister JA, Pingel ES, Jadwin-Cakmak L, Harper GW, Horvath K, Weiss G, Dittus P. Acceptability and preliminary efficacy of a tailored online HIV/STI testing intervention for young men who have sex with men: the Get Connected! program. *AIDS Behav*. 2015;19:1860-74; PMCID: PMC4522230.
74. Bailey J, Mann S, Wayal S, Abraham C, Murray E. Digital media interventions for sexual health promotion-opportunities and challenges: a great way to reach people, particularly those at increased risk of sexual ill health. *BMJ*. 2015;350:h1099.
75. Gabarron E, Wynn R. Use of social media for sexual health promotion: a scoping review. *Global Health Action*. 2016;9.
76. Brown CH, Mohr DC, Gallo CG, Mader C, Palinkas L, Wingood G, Prado G, Kellam SG, Pantin H, Poduska J, Gibbons R, McManus J, Ogihara M, Valente T, Wulczyn F, Czaja S, Sutcliffe G, Villamar J, Jacobs C. A computational

future for preventing HIV in minority communities: how advanced technology can improve implementation of effective programs. *J Acquir Immune Defic Syndr*. 2013;63 Suppl 1:S72-84; PMCID: 3746769.
77. National Center for HIV/AIDS VH, Sexually Transmitted Disease, and Tuberculosis Prevention. Comprehensive High-Impact HIV Prevention Projects for Community-Based Organizations: CDC-RFA-PS15-1502. Atlanta, GA: Centers for Disease Control and Prevention, 2014.
78. Du Bois SN, Johnson SE, Mustanski B. Examining racial and ethnic minority differences among YMSM during recruitment for an online HIV prevention intervention study. *AIDS Behav*. 2012;16:1430-5; PMCID: PMC3288566.
79. Weinhardt LS, Carey MP, Johnson BT, Bickham NL. Effects of HIV counseling and testing on sexual risk behavior: A meta-analytic review of published research, 1985-1997. *Am J Public Health*. 1999;89:1397-405.
80. Kamb ML, Fishbein M, Douglas JM, Jr., Rhodes F, Rogers J, Bolan G, Zenilman J, Hoxworth T, Malotte CK, Iatesta M, Kent C, Lentz A, Graziano S, Byers RH, Peterman TA. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: A randomized controlled trial. Project RESPECT Study Group. *JAMA*. 1998;280:1161-7.
81. Fernyak SE, Page-Shafer K, Kellogg TA, McFarland W, Katz MH. Risk behaviors and HIV incidence among repeat testers at publicly funded HIV testing sites in San Francisco. *J Acquir Immune Defic Syndr*. 2002;31:63-70.
82. Feinstein BA, Johnson BA, Parsons JT, Mustanski B. Reactions to Testing HIV Negative: Measurement and Associations with Sexual Risk Behaviour Among Young MSM Who Recently Tested HIV Negative. *AIDS Behav*. 2016:1-11.
83. Mustanski B, Rendina HJ, Greene GJ, Sullivan PS, Parsons JT. Testing negative means I'm lucky, making good choices, or immune: diverse reactions to HIV test results are associated with risk behaviors. *Ann Behav Med*. 2014;48:371-83; PMCID: PMC4224993.
84. Silvestre AJ, Gehl MB, Encandela J, Schelzel G. A participant observation study using actors at 30 publicly funded HIV counseling and testing sites in Pennsylvania. *Am J Public Health*. 2000;90:1096-9.
85. Doll M, Fortenberry J, Roseland D, McAuliff K, Wilson C, Boyer C. Linking HIV-Negative Youth to Prevention Services in 12 U.S. Cities: Barriers and Facilitators to Implementing the HIV Prevention Continuum. *J Adolesc Health*. 2017.
86. Fisher JD, Fisher WA, Williams SS, Malloy TE. Empirical tests of an information-motivation-behavioral skills model of AIDS-preventive behavior with gay men and heterosexual university students. *Health Psychol*. 1994;13:238-50.
87. Fisher JD, Fisher WA. The information-motivation-behavioral skills model. In: DiClemente RJ, Crosby RA, Kegler MC, editors. Emerging theories in health promotion practice and research: Strategies for improving public health. San Francisco: Jossey-Bass; 2002. p. 40-70.
88. Fisher CM. Are information, motivation, and behavioral skills linked with HIV-related sexual risk among young men who have sex with men? *Journal of HIV/AIDS & Social Services*. 2011;10:5 - 21.
89. Marlatt GA, Donovan DM. Relapse prevention: maintenance strategies in the treatment of addictive behaviors. 2nd ed. New York: Guilford Press; 2005. 416 p.
90. Herbst JH, Sherba RT, Crepaz N, Deluca JB, Zohrabyan L, Stall RD, Lyles CM, Team HAPRS. A meta-analytic review of HIV behavioral interventions for reducing sexual risk behavior of men who have sex with men. *J Acquir Immune Defic Syndr*. 2005;39:228-41.
91. Albarracin D, Gillette JC, Earl AN, Glasman LR, Durantini MR, Ho MH. A test of major assumptions about behavior change: a comprehensive look at the effects of passive and active HIV-prevention interventions since the beginning of the epidemic. *Psychol Bull*. 2005;131:856-97.
92. Holloway IW, Dougherty R, Gildner J, Beougher SC, Pulsipher C, Montoya JA, Plant A, Leibowitz A. Brief Report: PrEP Uptake, Adherence, and Discontinuation Among California YMSM Using Geosocial Networking Applications. *J Acquir Immune Defic Syndr*. 2017;74:15-20; PMCID: PMC5140696.
93. Parsons JT, Rendina HJ, Lassiter JM, Whitfield TH, Starks TJ, Grov C. Uptake of HIV Pre-Exposure Prophylaxis (PrEP) in a National Cohort of Gay and Bisexual Men in the United States. *J Acquir Immune Defic Syndr*. 2017;74:285-92; PMCID: PMC5315535.

94. Strauss BB, Greene GJ, Phillips G, 2nd, Bhatia R, Madkins K, Parsons JT, Mustanski B. Exploring Patterns of Awareness and Use of HIV Pre-Exposure Prophylaxis Among Young Men Who Have Sex with Men. *AIDS Behav*. 2017;21:1288-98; PMCID: PMC5226918.
95. Kessler RS, Purcell EP, Glasgow RE, Klesges LM, Benkeser RM, Peek CJ. What does it mean to "employ" the RE-AIM model? *Eval Health Prof*. 2013;36:44-66.
96. Gaglio B, Shoup JA, Glasgow RE. The RE-AIM framework: a systematic review of use over time. *Am J Public Health*. 2013;103:e38-46; PMCID: PMC3698732.
97. Bennett GG, Glasgow RE. The delivery of public health interventions via the Internet: actualizing their potential. *Annu Rev Public Health*. 2009;30:273-92.
98. Glasgow RE, Phillips SM, Sanchez MA. Implementation science approaches for integrating eHealth research into practice and policy. *Int J Med Inform*. 2014;83:e1-11.
99. Glasgow RE, Eckstein ET, ElZarrad MK. Implementation science perspectives and opportunities for HIV/AIDS research: Integrating science, practice, and policy. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2013;63:S26-S31.
100. Palinkas LA, Spear SE, Mendon SJ, Villamar J, Brown CH. Development of a system for measuring sustainment of prevention programs and initiatives. Society for Implementation Research Collaboration; Seattle, WA2017.
101. Golub SA, Gamarel KE. The impact of anticipated HIV stigma on delays in HIV testing behaviors: findings from a community-based sample of men who have sex with men and transgender women in New York City. *AIDS Patient Care STDS*. 2013;27:621-7; PMCID: PMC3820140.
102. Schwarcz S, Richards TA, Frank H, Wenzel C, Hsu LC, Chin CS, Murphy J, Dilley J. Identifying barriers to HIV testing: personal and contextual factors associated with late HIV testing. *AIDS Care*. 2011;23:892-900.
103. Siedner MJ, Ng CK, Bassett IV, Katz IT, Bangsberg DR, Tsai AC. Trends in CD4 count at presentation to care and treatment initiation in sub-Saharan Africa, 2002-2013: a meta-analysis. *Clin Infect Dis*. 2015;60:1120-7; PMCID: PMC4366582.
104. Conway DP, Holt M, Couldwell DL, Smith DE, Davies SC, McNulty A, Keen P, Cunningham P, Guy R, on behalf of the Sydney Rapid HIVTS. Barriers to HIV testing and characteristics associated with never testing among gay and bisexual men attending sexual health clinics in Sydney. *Journal of the International AIDS Society*. 2015;18:20221.
105. Deblonde J, De Koker P, Hamers F, Fontaine JC, Luchters S, Temmerman M. Barriers to HIV testing in Europe: a systematic review. *European Journal of Public Health*. 2010;20:422-32.
106. Lippman SA, Moran L, Sevelius J, Castillo LS, Ventura A, Treves-Kagan S, Buchbinder S. Acceptability and Feasibility of HIV Self-Testing Among Transgender Women in San Francisco: A Mixed Methods Pilot Study. *AIDS Behav*. 2016;20:928-38; PMCID: PMC4799740.
107. de la Fuente L, Rosales-Statkus ME, Hoyos J, Pulido J, Santos S, Bravo MJ, Barrio G, Fernández-Balbuena S, Belza MJ, the Madrid Rapid HIVTG. Are Participants in a Street-Based HIV Testing Program Able to Perform Their Own Rapid Test and Interpret the Results? *PLoS ONE*. 2012;7:e46555.
108. Bustamante MJ, Konda KA, Joseph Davey D, Leon SR, Calvo GM, Salvatierra J, Brown B, Caceres CF, Klausner JD. HIV self-testing in Peru: questionable availability, high acceptability but potential low linkage to care among men who have sex with men and transgender women. *Int J STD AIDS*. 2017;28:133-7.
109. Tao J, Li MY, Qian HZ, Wang LJ, Zhang Z, Ding HF, Ji YC, Li DL, Xiao D, Hazlitt M, Vermund SH, Xiu X, Bao Y. Home-based HIV testing for men who have sex with men in China: a novel community-based partnership to complement government programs. *PLoS ONE*. 2014;9:e102812; PMCID: PMC4106852.
110. Krause J, Subklew-Sehume F, Kenyon C, Colebunders R. Acceptability of HIV self-testing: a systematic literature review. *BMC Public Health*. 2013;13:735; PMCID: PMC3750621.
111. Figueroa C, Johnson C, Verster A, Baggaley R. Attitudes and Acceptability on HIV Self-testing Among Key Populations: A Literature Review. *AIDS Behav*. 2015;19:1949-65; PMCID: PMC4598350.

112. Witzel TC, Rodger AJ, Burns FM, Rhodes T, Weatherburn P. HIV Self-Testing among Men Who Have Sex with Men (MSM) in the UK: A Qualitative Study of Barriers and Facilitators, Intervention Preferences and Perceived Impacts. *PLoS ONE*. 2016;11:e0162713.
113. Johnson C, Kennedy C, Fonner V, Siegfried N, Figueroa C, Dalal S, Sands A, Baggaley R. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. *JIAS*. 2017;20:21594.
114. Shih SL, Graseck AS, Secura GM, Peipert JF. Screening for STIs at Home or in the Clinic? *Curr Opin Infect Dis*. 2011;24:78-84.
115. Neumann MS, Sogolow E. Replicating effective programs: HIV/AIDS prevention technology transfer. *AIDS Education & Prevention*. 2000;12:35-48.
116. Wilson MG, Rourke SB, Lavis JN, Bacon J, Travers R. Community capacity to acquire, assess, adapt, and apply research evidence: a survey of Ontario's HIV/AIDS sector. *Implement Sci*. 2011;6:54; PMCID: PMC3123230.
117. Leeman J, Calancie L, Hartman MA, Escoffery CT, Herrmann AK, Tague LE, Moore AA, Wilson KM, Schreiner M, Samuel-Hodge C. What strategies are used to build practitioners' capacity to implement community-based interventions and are they effective?: a systematic review. *Implement Sci*. 2015;10:80; PMCID: PMC4449971.
118. Bauer MS, Damschroder L, Hagedorn H, Smith J, Kilbourne AM. An introduction to implementation science for the non-specialist. *BMC Psychol*. 2015;3:32; PMCID: PMC4573926.
119. National Institutes of Health. Research methods resource: Group- or cluster-randomized trials (GRTs) Bethesda, MD: National Institutes of Health; 2017 [12 December 2017]. Available from: https://researchmethodsresources.nih.gov/grt.aspx.
120. Murray DM. Design and analysis of group-randomized trials. New York: Oxford University Press; 1998. xi, 467 p. p.
121. Brown CH, Wang W, Kellam SG, Muthen BO, Petras H, Toyinbo P, Poduska J, Ialongo N, Wyman PA, Chamberlain P, Sloboda Z, MacKinnon DP, Windham A, Prevention S, Methodology G. Methods for testing theory and evaluating impact in randomized field trials: Intent-to-treat analyses for integrating the perspectives of person, place, and time. *Drug Alcohol Depend*. 2008;95 Suppl 1:S74-S104; PMCID: PMC2560173.
122. Vermund SH, Fidler SJ, Ayles H, Beyers N, Hayes RJ. Can combination prevention strategies reduce HIV transmission in generalized epidemic settings in Africa? The HPTN 071 (PopART) study plan in South Africa and Zambia. *J Acquir Immune Defic Syndr*. 2013;63 Suppl 2:S221-7; PMCID: PMC3739051.
123. Coates TJ, Kulich M, Celentano DD, Zelaya CE, Chariyalertsak S, Chingono A, Gray G, Mbwambo JKK, Morin SF, Richter L, Sweat M, van Rooyen H, McGrath N, Fiamma A, Laeyendecker O, Piwowar-Manning E, Szekeres G, Donnell D, Eshleman SH. Effect of community-based voluntary counselling and testing on HIV incidence and social and behavioural outcomes (NIMH Project Accept; HPTN 043): a cluster-randomised trial. *The Lancet Global Health*. 2014;2:e267-e77.
124. Glassman JR, Potter SC, Baumler ER, Coyle KK. Estimates of Intraclass Correlation Coefficients From Longitudinal Group-Randomized Trials of Adolescent HIV/STI/Pregnancy Prevention Programs. *Health Education & Behavior*. 2015;42:545-53.
125. Witte SS, Wu E, El-Bassel N, Hunt T, Gilbert L, Medina KP, Chang M, Kelsey R, Rowe J, Remien R. Implementation of a couple-based HIV prevention program: a cluster randomized trial comparing manual versus Web-based approaches. *Implement Sci*. 2014;9:116; PMCID: PMC4172848.
126. Durlak JA, DuPre EP. Implementation matters: a review of research on the influence of implementation on program outcomes and the factors affecting implementation. *Am J Community Psychol*. 2008;41:327-50.
127. Baker TB, Gustafson DH, Shah D. How can research keep up with eHealth? Ten strategies for increasing the timeliness and usefulness of eHealth research. *J Med Internet Res*. 2014;16:e36; PMCID: PMC3961695.
128. Murray E, Burns J, May C, Finch T, O'Donnell C, Wallace P, Mair F. Why is it difficult to implement e-health initiatives? A qualitative study. *Implement Sci*. 2011;6:6; PMCID: PMC3038974.

129. Palinkas LA, Holloway IW, Rice E, Brown CH, Valente TW, Chamberlain P. Influence network linkages across implementation strategy conditions in a randomized controlled trial of two strategies for scaling up evidence-based practices in public youth-serving systems. *Implement Sci*. 2013;8:133; PMCID: 3930152.
130. Clerkin EM, Newcomb ME, Mustanski B. Unpacking the racial disparity in HIV rates: the effect of race on risky sexual behavior among Black young men who have sex with men (YMSM). *J Behav Med*. 2011;34:237-43; PMCID: Not relevant to NIH public access policy.
131. Mustanski B, Newcomb ME, Clerkin EM. Relationship characteristics and sexual risk-taking in young men who have sex with men. *Health Psychology*. 2011;30:597-605; PMCID: PMC3184611.
132. Newcomb ME, Clerkin EM, Mustanski B. Sensation seeking moderates the effects of alcohol and drug use prior to sex on sexual risk in young men who have sex with men. *AIDS Behav*. 2011;15:565-75; PMCID: Not relevant to NIH public access policy.
133. Liu RT, Mustanski B. Suicidal ideation and self-harm in lesbian, gay, bisexual, and transgender youth. *Am J Prev Med*. 2012;42:221-8; PMCID: Not relevant to NIH public access policy.
134. Newcomb ME, Ryan DT, Garofalo R, Mustanski B. Race-based sexual stereotypes and their effects on sexual risk behavior in racially diverse young men who have sex with men. *Arch Sex Behav*. 2015;44:1959-68; PMCID: 4561004.
135. Reuter T, Newcomb ME, Whitton SW, Mustanski B. Intimate partner violence victimization in LGBT young adults: demographic differences and associations with health behaviors. *Psychology of Violence*. In Press.
136. Garofalo R, Herrick A, Mustanski BS, Donenberg GR. Tip of the iceberg: young men who have sex with men, the Internet, and HIV risk. *Am J Public Health*. 2007;97:1113-7; PMCID: PMC1874202.
137. Mustanski B. Are sexual partners met online associated with HIV/STI risk behaviours? Retrospective and daily diary data in conflict. *AIDS Care*. 2007;19:822-7; PMCID: Not relevant to NIH public access policy.
138. Mustanski B, Lyons T, Garcia SC. Internet use and sexual health of young men who have sex with men: a mixed-methods study. *Arch Sex Behav*. 2011;40:289-300; PMCID: PMC2914836.
139. Magee JC, Bigelow L, Dehaan S, Mustanski BS. Sexual health information seeking online: a mixed-methods study among lesbian, gay, bisexual, and transgender young people. *Health Educ Behav*. 2012;39:276-89; PMCID: Not relevant to NIH public access policy.
140. DeHaan S, Kuper LE, Magee JC, Bigelow L, Mustanski BS. The interplay between online and offline explorations of identity, relationships, and sex: a mixed-methods study with LGBT youth. *J Sex Res*. 2013;50:421-34; PMCID: Not relevant to NIH public access policy.
141. Ybarra ML, DuBois LZ, Parsons JT, Prescott TL, Mustanski B. Online Focus Groups as an HIV Prevention Program for Gay, Bisexual, and Queer Adolescent Males. *AIDS Educ Prev*. 2014;26:554-64; PMCID: PMC4379702.
142. Mustanski B, Greene GJ, Ryan D, Whitton SW. Feasibility, acceptability, and initial efficacy of an online sexual health promotion program for LGBT youth: the Queer Sex Ed intervention. *J Sex Res*. 2015;52:220-30; PMCID: Not relevant to NIH public access policy.
143. Newcomb ME, Swann G, Mohr D, Mustanski B. Do Diary Studies Cause Behavior Change? An Examination of Reactivity in Sexual Risk and Substance Use in Young Men Who Have Sex with Men. *AIDS Behav*. 2018.
144. Mustanski B. A pragmatic trial of an adaptive eHealth HIV prevention program for diverse adolescent MSM (1U01MD011281). National Institute on Minority Health and Health Disparities; 2016-2021.
145. Ybarra ML, Prescott TL, Philips GL, 2nd, Bull SS, Parsons JT, Mustanski B. Iteratively developing an mHealth HIV orevention program for sexual minority adolescent men. *AIDS Behav*. 2016;20:1157-72; PMCID: PMC4740246.
146. Fisher JD, Fisher WA. Theoretical approaches to individual-level change in HIV risk behavior. In: Peterson JL, DiClemente RJ, editors. Handbook of HIV Prevention. New York: Klewer Academic/Plenum Publishers; 2000.
147. Fisher JD, Fisher WA. Changing AIDS-risk behavior. *Psychol Bull*. 1992;111:455-74.
148. Clark RC, Mayer RE. E-Learning and the science of instruction: proven guidelines for consumers and designers of multimedia learning. San Francisco, CA: Jossey-Bass/Pfeiffer; 2003. 322 p.
149. Herbst JH, Beeker C, Mathew A, McNally T, Passin WF, Kay LS, Crepaz N, Lyles CM, Briss P, Chattopadhyay S, Johnson RL, Task Force on Community Preventive S. The effectiveness of individual-, group-, and community-

level HIV behavioral risk-reduction interventions for adult men who have sex with men: a systematic review. *Am J Prev Med*. 2007;32:S38-67.
150. Johnson WD, Holtgrave DR, McClellan WM, Flanders WD, Hill AN, Goodman M. HIV intervention research for men who have sex with men: a 7-year update. *AIDS Educ Prev*. 2005;17:568-89.
151. Johnson WD, Diaz RM, Flanders WD, Goodman M, Hill AN, Holtgrave D, Malow R, McClellan WM. Behavioral interventions to reduce risk for sexual transmission of HIV among men who have sex with men. *Cochrane Database Syst Rev*. 2008:CD001230.
152. Tarnowski KJ, Simonian SJ. Assessing treatment acceptability: The abbreviated acceptability rating profile. *J Behav Ther Exp Psychiatry*. 1992;23:101-6.
153. Greene GJ, Madkins K, Dispenza J, Andrews R, Mustanski B. Evaluating an online HIV prevention intervention from a translational science perspective: Findings from an academic-community partnership. American Evaluation Association; Chicago, IL2015, November.
154. Mustanski B, Madkins K, Greene GJ, Parsons J, Sullivan P. Keep It Up! (KIU!): Lessons on maximizing recruitment, engagement, and impact with diverse men who have sex with men. National HIV Prevention Conference; Atlanta, GA: Centers for Disease Control and Prevention; 2015.
155. Fisher CB, Fried AL, Desmond M, Macapagal K, Mustanski B. Facilitators and Barriers to Participation in PrEP HIV Prevention Trials Involving Transgender Male and Female Adolescents and Emerging Adults. *AIDS Educ Prev*. 2017;29:205-17.
156. Feinstein BA, Moody RL, John SA, Parsons JT, Mustanski B. A three-city comparison of drug use and drug use before sex among young men who have sex with men in the United States. *Journal of Gay & Lesbian Social Services*. 2018;30:82-101.
157. Mustanski B. Results from the Keep It Up! 2.0 RCT: An eHealth intervention significantly reduces biological and behavioral markers of HIV risk in diverse young MSM. Centers for Disease Control and Prevention Division of HIV Prevention Translating Research into Practice (TRIP) Seminar Series; Atlanta, GA2017.
158. Ryan GW, Bernard HR. Techniques to identify themes. *Field Methods*. 2003;15:85.
159. Schueller SM, Begale M, Penedo FJ, Mohr DC. Purple: A Modular System for Developing and Deploying Behavioral Intervention Technologies. *Journal of Medical Internet Research*. 2014;16:e181.
160. Ben-Zeev D, Brenner CJ, Begale M, Duffecy J, Mohr DC, Mueser KT. Feasibility, acceptability, and preliminary efficacy of a smartphone intervention for schizophrenia. *Schizophr Bull*. 2014;40:1244-53; PMCID: PMC4193714.
161. Ben-Zeev D, Schueller SM, Begale M, Duffecy J, Kane JM, Mohr DC. Strategies for mHealth research: lessons from 3 mobile intervention studies. *Adm Policy Ment Health*. 2015;42:157-67; PMCID: PMC4232479.
162. Duffecy J, Sanford S, Wagner L, Begale M, Nawacki E, Mohr DC. Project onward: an innovative e-health intervention for cancer survivors. *Psychooncology*. 2013;22:947-51; PMCID: PMC3387296.
163. Mohr DC, Duffecy J, Jin L, Ludman EJ, Lewis A, Begale M, McCarthy M, Jr. Multimodal e-mental health treatment for depression: a feasibility trial. *J Med Internet Res*. 2010;12:e48; PMCID: PMC3057313.
164. Yanez B, McGinty HL, Mohr DC, Begale MJ, Dahn JR, Flury SC, Perry KT, Penedo FJ. Feasibility, acceptability, and preliminary efficacy of a technology-assisted psychosocial intervention for racially diverse men with advanced prostate cancer. *Cancer*. 2015;121:4407-15; PMCID: PMC4670576.
165. Burns MN, Montague E, Mohr DC. Initial design of culturally informed behavioral intervention technologies: developing an mHealth intervention for young sexual minority men with generalized anxiety disorder and major depression. *J Med Internet Res*. 2013;15:e271; PMCID: 3869054.
166. Wingood GM, DiClemente RJ. The ADAPT-ITT model: a novel method of adapting evidence-based HIV Interventions. *J Acquir Immune Defic Syndr*. 2008;47 Suppl 1:S40-6.
167. Kelly JA, Heckman TG, Stevenson LY, Williams PN, Ertl T, Hays RB, Leonard NR, O'Donnell L, Terry MA, Sogolow ED, Neumann MS. Transfer of research-based HIV prevention interventions to community service providers: fidelity and adaptation. *AIDS Educ Prev*. 2000;12:87-98.

168. Mustanski B, Garofalo R, Herrick A, Donenberg G. Psychosocial health problems increase risk for HIV among urban young men who have sex with men: preliminary evidence of a syndemic in need of attention. *Ann Behav Med*. 2007;34:37-45; PMCID: PMC2219199.
169. Stall R, Friedman M, Catania J. Interacting epidemics and gay men's health: a theory of syndemic production among urban gay men. Oxford, UK: Oxford University Press; 2007.
170. Herrick A, Stall R, Egan J, Schrager S, Kipke M. Pathways towards risk: Syndemic conditions mediate the effect of adversity on HIV risk behaviors among young men who have sex with men (YMSM). *J Urban Health*. 2014;91:969-82; PMCID: 4199441.
171. Mustanski B, Andrews R, Herrick A, Stall R, Schnarrs PW. A syndemic of psychosocial health disparities and associations with risk for attempting suicide among young sexual minority men. *Am J Public Health*. 2014;104:287-94; PMCID: PMC3935701.
172. Mustanski B, Phillips G, 2nd, Ryan DT, Swann G, Kuhns L, Garofalo R. Prospective Effects of a Syndemic on HIV and STI Incidence and Risk Behaviors in a Cohort of Young Men Who Have Sex with Men. *AIDS Behav*. 2017;21:845-57; PMCID: PMC5303540.
173. Ybarra ML, Prescott TL, Phillips GL, 2nd, Bull SS, Parsons JT, Mustanski B. Pilot RCT Results of an mHealth HIV Prevention Program for Sexual Minority Male Adolescents. *Pediatrics*. 2017;140; PMCID: PMC5495523.
174. Gardner BS. Responsive Web Design: Enriching the User Experience. *Connectivity and the User Experience*. 2011;11:13.
175. Pew Internet & American Life Project. Teens and Technology 2013. 2013.
176. Mohr DC, Schueller SM, Riley WT, Brown CH, Cuijpers P, Duan N, Kwasny MJ, Stiles-Shields C, Cheung K. Trials of Intervention Principles: Evaluation Methods for Evolving Behavioral Intervention Technologies. *J Med Internet Res*. 2015;17:e166; PMCID: PMC4526981.
177. Rotheram-Borus MJ, Swendeman D, Chorpita BF. Disruptive innovations for designing and diffusing evidence-based interventions. *Am Psychol*. 2012;67:463-76.
178. Aarons GA, Sklar M, Mustanski B, Benbow N, Brown CH. "Scaling-out" evidence-based interventions to new populations or new health care delivery systems. *Implement Sci*. 2017;12:111; PMCID: PMC5588712.
179. Titov N, Dear BF, Staples LG, Bennett-Levy J, Klein B, Rapee RM, Shann C, Richards D, Andersson G, Ritterband L, Purtell C, Bezuidenhout G, Johnston L, Nielssen OB. MindSpot Clinic: An Accessible, Efficient, and Effective Online Treatment Service for Anxiety and Depression. *Psychiatr Serv*. 2015;66:1043-50.
180. Landsverk J, Brown CH, Chamberlain P, Palinkas L, Ogihara M, Czaja S, Goldhaber-Fiebert JD, Rolls Reutz JA, Horwitz SM. Design and Analysis in Dissemination and Implementation Research. Dissemination and Implementation Research in HealthTranslating Science to Practice2012. p. 225-60.
181. Brown CH, Liao J. Principles for designing randomized preventive trials in mental health: an emerging developmental epidemiology paradigm. *Am J Community Psychol*. 1999;27:673-710.
182. Brown C, Chamberlain P, Saldana L, Padgett C, Wang W, Cruden G. Evaluation of two implementation strategies in 51 child county public service systems in two states: results of a cluster randomized head-to-head implementation trial. *Implement Sci*. 2014;9:134; PMCID: 4201704.
183. Knight DK, Belenko S, Wiley T, Robertson AA, Arrigona N, Dennis M, Bartkowski JP, McReynolds LS, Becan JE, Knudsen HK, Wasserman GA, Rose E, DiClemente R, Leukefeld C, Cooperative J-T. Juvenile Justice-Translational Research on Interventions for Adolescents in the Legal System (JJ-TRIALS): a cluster randomized trial targeting system-wide improvement in substance use services. *Implement Sci*. 2016;11:57; PMCID: PMC4850663.
184. Friedman LM, Furberg C, DeMets DL. Fundamentals of clinical trials. 4th ed. New York: Springer; 2010. xviii, 445 p. p.
185. Phillips G, 2nd, Birkett M, Hammond S, Mustanski B. Partner Preference Among Men Who Have Sex with Men: Potential Contribution to Spread of Human Immunodeficiency Virus Within Minority Populations. *LGBT Health*. 2016.
186. Newcomb ME, Mongrella MC, Weis B, McMillen SJ, Mustanski B. Partner Disclosure of PrEP Use and Undetectable Viral Load on Geosocial Networking Apps: Frequency of Disclosure and Decisions About Condomless Sex. *J Acquir Immune Defic Syndr*. 2016;71:200-6; PMCID: 4712713.

187. Macapagal K, Coventry R, Puckett JA, Phillips G, Mustanski B. Geosocial Networking App Use Among Men Who Have Sex With Men in Serious Romantic Relationships. *Arch Sex Behav*. 2016;45:1513-24.
188. Gerend MA, Madkins K, Phillips 2nd G, Mustanski B. Predictors of Human Papillomavirus Vaccination Among Young Men Who Have Sex With Men. *Sex Transm Dis*. 2016;43:185-91.
189. Mustanski B, Ryan DT, Sanchez T, Sineath C, Macapagal K, Sullivan PS. Effects of messaging about multiple biomedical and behavioral HIV prevention methods on intentions to use among US MSM: results of an experimental messaging study. *AIDS Behav*. 2014;18:1651-60; PMCID: PMC4127150.
190. Grey JA, Konstan J, Iantaffi A, Wilkerson JM, Galos D, Rosser BR. An updated protocol to detect invalid entries in an online survey of men who have sex with men (MSM): how do valid and invalid submissions compare? *AIDS Behav*. 2015;19:1928-37.
191. Bauermeister J, Pingel E, Zimmerman M, Couper M, Carballo-Dieguez A, Strecher VJ. Data Quality in web-based HIV/AIDS research: Handling Invalid and Suspicious Data. *Field methods*. 2012;24:272-91; PMCID: PMC3505140.
192. Mustanski BS. Getting wired: Exploiting the Internet for the collection of valid sexuality data. *J Sex Res*. 2001;38:292-301.
193. Mustanski BS. Methodological issues in online sexual health research. In: Liamputtong P, editor. Health research in cyberspace: Methodological, practical and personal experiences in doing health and social science researching online: Nova Science Publishers, Inc.; 2006. p. Chapter 7.
194. Konstan JA, Rosser BRS, Ross MW, Stanton J, Edwards WM. The story of Subject Naught: A cautionary but optimistic tale of internet survey research. *Journal of Computer-Mediated Communication*. 2005;10.
195. OraSure Technologies. OraQuick In-Home HIV test - Package Insert. 2012.
196. Huang E, Marlin RW, Young SD, Medline A, Klausner JD. Using Grindr, a Smartphone Social-Networking Application, to Increase HIV Self-Testing Among Black and Latino Men Who Have Sex With Men in Los Angeles, 2014. *AIDS Educ Prev*. 2016;28:341-50.
197. Young SD, Daniels J, Chiu CJ, Bolan RK, Flynn RP, Kwok J, Klausner JD. Acceptability of using electronic vending machines to deliver oral rapid HIV self-testing kits: a qualitative study. *PLoS ONE*. 2014;9:e103790; PMCID: PMC4116256.
198. Sharma A, Chavez PR, MacGowan RJ, McNaghten AD, Mustanski B, Gravens L, Freeman AE, Sullivan PS. Willingness to distribute free rapid home HIV test kits and to test with social or sexual network associates among men who have sex with men in the United States. *AIDS Care*. 2017;29:1499-503.
199. Tregear SJ, Sullivan P, Mustanski B, Chiasson MA. Evaluation of Rapid HIV Self-Testing among MSM in High Prevalence Cities. 2011-N-13417. Centers for Disease Control and Prevention; 2011-2015.
200. Lippman SA, Veloso VG, Buchbinder S, Fernandes NM, Terto V, Sullivan PS, Grinsztejn B. Over-the-counter human immunodeficiency virus self-test kits: time to explore their use for men who have sex with men in Brazil. *Braz J Infect Dis*. 2014;18:239-44.
201. Landsverk J, Brown CH, Smith JD, Chamberlain P, Curran GM, Palinkas L, Vermeer W, Ogihara M, Czaja S, Goldhaber-Fiebert JD, Rolls Reutz JA, Horwitz SM. Design and Analysis in Dissemination and Implementation Research. In: Brownson R, Colditz G, Proctor E, editors. Dissemination and Implementation Research in Health: Translating Science to Practice. 2nd ed. Oxford, UK: Oxford University Press; 2018.
202. Chamberlain P, Saldana L, Brown CH, Leve L. Implementation of Multidimensional Treatment Foster Care in California: A randomized control trial of an evidence-based practice. In: Roberts-DeGennaro M, Fogel SJ, editors. Using Evidence to Inform Practice for Community and Organizational Change. Chicago, IL: Lyceum Books; 2011. p. 218-34.
203. Brown CH, Chamberlain P, Saldana L, Padgett C, Wang W, Cruden G. Evaluation of two implementation strategies in 51 child county public service systems in two states: results of a cluster randomized head-to-head implementation trial. *Implementation science : IS*. 2014;9:134; PMCID: PMC4201704.
204. Chamberlain P, Brown CH, Saldana L. Observational measure of implementation progress in community based settings: the Stages of Implementation Completion (SIC). *Implement Sci*. 2011;6:116; PMCID: 3197550.

205. Gallo C, Pantin H, Villamar J, Prado G, Tapia M, Ogihara M, Cruden G, Brown CH. Blending Qualitative and Computational Linguistics Methods for Fidelity Assessment: Experience with the Familias Unidas Preventive Intervention. *Adm Policy Ment Health*. 2015;42:574-85; PMCID: PMC4125546.
206. Saldana L, Chamberlain P, Wang W, Hendricks Brown C. Predicting program start-up using the stages of implementation measure. *Adm Policy Ment Health*. 2012;39:419-25; PMCID: PMC3212640.
207. Spoth R, Rohrbach LA, Greenberg M, Leaf P, Brown CH, Fagan A, Catalano RF, Pentz MA, Sloboda Z, Hawkins JD, Society for Prevention Research Type 2 Translational Task Force M, Contributing A. Addressing core challenges for the next generation of type 2 translation research and systems: the translation science to population impact (TSci Impact) framework. *Prev Sci*. 2013;14:319-51; PMCID: 3696461.
208. St George SM, Huang S, Vidot DC, Smith JD, Brown CH, Prado G. Factors associated with the implementation of the Familias Unidas intervention in a type 3 translational trial. *Translational behavioral medicine*. 2016;6:105-14; PMCID: PMC4807187.
209. Valente TW, Palinkas LA, Czaja S, Chu KH, Brown CH. Social network analysis for program implementation. *PLoS One*. 2015;10:e0131712; PMCID: PMC4482437.
210. Wejnert C, Hess KL, Rose CE, Balaji A, Smith JC, Paz-Bailey G, Group NS. Age-Specific Race and Ethnicity Disparities in HIV Infection and Awareness Among Men Who Have Sex With Men-20 US Cities, 2008-2014. *J Infect Dis*. 2016;213:776-83.
211. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, Goicochea P, Casapia M, Guanira-Carranza JV, Ramirez-Cardich ME, Montoya-Herrera O, Fernandez T, Veloso VG, Buchbinder SP, Chariyalertsak S, Schechter M, Bekker LG, Mayer KH, Kallas EG, Amico KR, Mulligan K, Bushman LR, Hance RJ, Ganoza C, Defechereux P, Postle B, Wang F, McConnell JJ, Zheng JH, Lee J, Rooney JF, Jaffe HS, Martinez AI, Burns DN, Glidden DV. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363:2587-99.
212. Smith DK, Herbst JH, Zhang X, Rose CE. Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the United States. *J Acquir Immune Defic Syndr*. 2015;68:337-44.
213. Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G, Kiarie J, Inambao M, Kilembe W, Farquhar C, Celum C, Partners in Prevention HSVHIVTST. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. *J Infect Dis*. 2012;205:358-65; PMCID: PMC3256946.
214. Goodreau SM, Rosenberg ES, Jenness SM, Luisi N, Stansfield SE, Millett GA, Sullivan PS. Sources of racial disparities in HIV prevalence in men who have sex with men in Atlanta, GA, USA: a modelling study. *The Lancet HIV*. 2017.
215. Hedeker D, Gibbons RD, Flay BR. Random-effects regression models for clustered data with an example from smoking prevention research. *J Consult Clin Psychol*. 1994;62:757-65.
216. Mustanski B, Starks T, Newcomb ME. Methods for the design and analysis of relationship and partner effects on sexual health. *Arch Sex Behav*. 2014;43:21-33; PMCID: PMC3924882.
217. 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. *J Am Acad Child Adolesc Psychiatry*. 2001;40:642-53; PMCID: PMC1201503.
218. Mustanski B, Ryan DT, Garofalo R. Associations of sexually transmitted infections with condom problems among young men who have sex with men. *Sex Transm Dis*. 2014;41:427-32; PMCID: PMC4261919.
219. Newcomb ME, Mustanski B. Developmental change in the relationship between alcohol and drug use before sex and sexual risk behavior in young men who have sex with men. *AIDS Behav*. 2014;18:1981-90; PMCID: PMC4175054.
220. Newcomb ME, Ryan DT, Garofalo R, Mustanski B. The effects of sexual partnership and relationship characteristics on three sexual risk variables in young men who have sex with men. *Arch Sex Behav*. 2014;43:61-72; PMCID: PMC3891854.
221. Garofalo R, Gayles T, Bottone PD, Ryan D, Kuhns LM, Mustanski B. Racial/Ethnic Difference in HIV-related Knowledge among Young Men who have Sex with Men and their Association with Condom Errors. *Health Educ J*. 2015;74:518-30; PMCID: PMC4549001.

222. Garofalo R, Hotton AL, Kuhns LM, Gratzer B, Mustanski B. Incidence of HIV infection and Sexually Transmitted Infections and Related Risk Factors among Very Young Men Who Have Sex with Men. *J Acquir Immune Defic Syndr*. 2016;In Press; PMCID: PMC Journal in Process.
223. Garofalo R, Kuhns LM, Hidalgo M, Gayles T, Kwon S, Muldoon AL, Mustanski B. Impact of religiosity on the sexual risk behaviors of young men who have sex with men. *J Sex Res*. 2015;52:590-8; PMCID: PMC4425613.
224. Macapagal K, Greene GJ, Andrews R, Mustanski B. Evaluating the Relationship-Oriented Information, Motivation, and Behavioral Skills model of HIV preventive behaviors in young men who have sex with men. *AIDS Education & Prevention*. 2016;28:165-79.
225. Newcomb ME, Mustanski B. Developmental Change in the Effects of Sexual Partner and Relationship Characteristics on Sexual Risk Behavior in Young Men Who Have Sex with Men. *AIDS Behav*. 2015; PMCID: 4600632.
226. Newcomb ME, Ryan DT, Garofalo R, Mustanski B. Race-Based Sexual Stereotypes and Their Effects on Sexual Risk Behavior in Racially Diverse Young Men Who Have Sex with Men. *Arch Sex Behav*. 2015;44:1959-68.
227. Phillips G, Birkett M, Kuhns L, Hatchel T, Garofalo R, Mustanski B. Neighborhood-level associations with HIV infection among young men who have sex with men in Chicago. *Arch Sex Behav*. 2015;44:1773-86; PMCID: PMC4561028.
228. Ybarra ML, Prescott TL, Philips GL, 2nd, Bull SS, Parsons JT, Mustanski B. Iteratively Developing an mHealth HIV Prevention Program for Sexual Minority Adolescent Men. *AIDS Behav*. 2015;In Press; PMCID: 26238038.
229. Mustanski B, Newcomb M. Relationships and risk: Longitudinal analysis of relationship status and unprotected sex in young gay and bisexual men. Society for the Scientific Study of Sexuality; Las Vegas, NA2010.
230. Swann G, Newcomb ME, Mustanski B. Validation of the HIV Risk Assessment of Sexual Partnerships (H-RASP): Comparison to a 2-Month Prospective Diary Study. *Arch Sex Behav*. 2017;In Press.
231. Newcomb ME, Moran K, Feinstein BA, Forscher E, Mustanski B. Pre-Exposure Prophylaxis (PrEP) Use and Condomless Anal Sex: Evidence of Risk Compensation in a Cohort of Young Men Who Have Sex with Men. *J Acquir Immune Defic Syndr*. 2017.
232. Feinstein BA, Dellucci TV, Graham S, Parsons JT, Mustanski B. Sexually transmitted infections among young men who have sex with men: Experiences with diagnosis, treatment, and reinfection. *Sexuality Research and Social Policy*. 2018;in press.
233. Steen R, Wi TE, Kamali A, Ndowa F. Control of sexually transmitted infections and prevention of HIV transmission: mending a fractured paradigm. *Bull World Health Organ*. 2009;87:858-65; PMCID: 2770276.
234. Castillo R, Konda KA, Leon SR, Silva-Santisteban A, Salazar X, Klausner JD, Coates TJ, Cáceres CF. Human Immunodeficiency Virus (HIV) and Sexually Transmitted Infection (STI) incidence and associated risk factors among high-risk MSM and male-to-female transgender women in Lima, Peru. *JAIDS*. 2015;69:567-75.
235. Harawa NT, Holloway IW, Leibowitz A, Weiss R, Gildner J, Landovitz RJ, Perez MJ, Kulkarni S, Rotheram-Borus MJ, Shoptaw S. Serious concerns regarding a meta-analysis of preexposure prophylaxis use and STI acquisition. *AIDS*. 2017;31:739-40.
236. Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. *AIDS*. 2016;30:2251-2.
237. Kojima N, Davey DJ, Klausner JD. Addressing concerns regarding preexposure prophylaxis meta-analysis. *AIDS*. 2017;31:740-2.
238. Alaei K, Paynter CA, Juan SC, Alaei A. Using preexposure prophylaxis, losing condoms? Preexposure prophylaxis promotion may undermine safe sex. *AIDS*. 2016;30:2753-6.
239. Huhn GD, McIntyre AF, Broad JM, Holmes SW, Studzinski A, Rabins C, Dworkin MS. Factors associated with newly diagnosed HIV among persons with concomitant sexually transmitted diseases. *Sex Transm Dis*. 2008;35:731-7.
240. Chai SJ, Aumakhan B, Barnes M, Jett-Goheen M, Quinn N, Agreda P, Whittle P, Hogan T, Jenkins WD, Rietmeijer CA, Gaydos CA. Internet-based screening for sexually transmitted infections to reach nonclinic populations in the community: risk factors for infection in men. *Sex Transm Dis*. 2010;37:756-63; PMCID: 3187615.
241. Aptima Combo 2 Assay for Panther System Package Insert. San Diego, CA: Gen-Probe Incorporated; 2016.

242. Drummond MF, Schulpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Fourth ed. Oxford University Press2015.
243. Glick HA, Doshi JA, Sonnad SS, Polsky D. Economic evaluation in clinical trials: Oxford University Press; 2014.
244. Neumann PJ, Sanders GD, Russell LB, Siegel JE, Ganiats TG. Cost-Effectiveness in Health and Medicine. 2nd ed. New York, NY: Oxford University Press; 2017.
245. Polsky D, Glick H. Costing and cost analysis in randomized controlled trials: caveat emptor. *Pharmacoeconomics*. 2009;27:179-88; PMCID: PMC2971527.
246. (US) DoL. National compensation survey 2017 [24 December 2017]. Available from: http://www.bls.gov/data.
247. Okwundu CI, Uthman OA, Okoromah CA. Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals. *Cochrane Database Syst Rev*. 2012;7:CD007189.
248. Scott HM, Klausner JD. Sexually transmitted infections and pre-exposure prophylaxis: challenges and opportunities among men who have sex with men in the US. *AIDS Res Ther*. 2016;13:5; PMCID: PMC4719214.
249. Fiero MH, Huang S, Oren E, Bell ML. Statistical analysis and handling of missing data in cluster randomized trials: a systematic review. *Trials*. 2016;17:72; PMCID: PMC4748550.
250. Ten Have TR, Normand SL, Marcus SM, Brown CH, Lavori P, Duan N. Intent-to-Treat vs. Non-Intent-to-Treat Analyses under Treatment Non-Adherence in Mental Health Randomized Trials. *Psychiatr Ann*. 2008;38:772-83; PMCID: PMC2921714.
251. White IR, Horton NJ, Carpenter J, Pocock SJ. Strategy for intention to treat analysis in randomised trials with missing outcome data. *BMJ*. 2011;342:d40; PMCID: PMC3230114.
252. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *BMJ*. 1999;319:670-4; PMCID: PMC28218.
253. Graham JW. Missing data analysis: making it work in the real world. *Annu Rev Psychol*. 2009;60:549-76.
254. Reich NG, Myers JA, Obeng D, Milstone AM, Perl TM. Empirical power and sample size calculations for cluster-randomized and cluster-randomized crossover studies. *PLoS One*. 2012;7:e35564; PMCID: PMC3338707.
255. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41:1149-60.
256. Taveras S, Duncan T, Gentry D, Gilliam A, Kimbrough I, Minaya J. The evolution of the CDC HIV prevention capacity-building assistance initiative. *Journal of public health management and practice : JPHMP*. 2007;Suppl:S8-15.
257. Aarons GA, Hurlburt M, Horwitz SM. Advancing a conceptual model of evidence-based practice implementation in public service sectors. *Adm Policy Ment Health*. 2011;38:4-23; PMCID: 3025110.
258. Martinez RG, Lewis CC, Weiner BJ. Instrumentation issues in implementation science. *Implementation science : IS*. 2014;9:118; PMCID: PMC4164742.
259. DuBois LZ, Macapagal KR, Rivera Z, Prescott TL, Ybarra ML, Mustanski B. To have sex or not to have sex? An online focus group study of sexual decision making among sexually experienced and inexperienced gay and bisexual adolescent men. *Arch Sex Behav*. 2015;44:2027-40; PMCID: PMC4561008.
260. Kuper LE, Coleman BR, Mustanski BS. Coping With LGBT and Racial-Ethnic-Related Stressors: A Mixed-Methods Study of LGBT Youth of Color. *Journal of Research on Adolescence*. 2014;24:703-19; PMCID: PMC Journal - In Process.
261. Macapagal K, Greene GJ, Rivera Z, Mustanski B. "The best is always yet to come": Relationship stages and processes among young LGBT couples. *J Fam Psychol*. 2015;29:309-20; PMCID: PMC4644068.
262. Macapagal K, Matson M, Mustanski B. Using Dedoose for a multi-site, mixed-methods project on sexual and gender minority adolescent health. In: Salmona M, Lieber E, Kaczynski D, editors. Qualitative and Mixed Methods Data Analysis using Dedoose: A Practical Approach for Research across the Social Sciences. Thousand Oaks, CA: Sage; In Press.
263. Mustanski B, DuBois LZ, Prescott TL, Ybarra ML. A mixed-methods study of condom use and decision making among adolescent gay and bisexual males. *AIDS Behav*. 2014;18:1955-69; PMCID: PMC4174981.

264. Newcomb ME, Clifford A, Greene GJ, Mustanski B. Parent perspectives about sexual minority adolescent participation in research and requirements of parental permission. *J Adolesc Health*. 2016;59:443-9.
265. Motley DN, Hammond S, Mustanski B. Strategies Chosen by YMSM During Goal Setting to Reduce Risk for HIV and Other Sexually Transmitted Infections: Results From the Keep It Up! 2.0 Prevention Trial. *AIDS Educ Prev*. 2017;29:1-13.
266. Dedoose. User Guide 2016. Available from: http://dedoose.com/userguide.
267. Morgan DL. Qualitative content analysis: a guide to paths not taken. *Qual Health Res*. 1993;3:112-21.
268. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15:1277-88.
269. Corbin J, Strauss A. Basics of qualitative research: Techniques and procedures for developing grounded theory. 3rd ed. Thousand Oaks, CA, USA: SAGE Publications, Inc.; 2008.
270. Miles MB, Huberman AM. Qualitative Data Analysis: An Expanded Sourcebook. 2nd ed. Thousand Oaks: Sage Publications; 1994. xiv, 338 p. p.
271. NIH Office of Behavioral and Social Sciences. Best practices for mixed methods research in the health sciences. Bethesda: National Institutes of Health, 2018.
272. Aarons GA, Ehrhart MG, Farahnak LR. The implementation leadership scale (ILS): Development of a brief measure of unit level implementation leadership. *Implementation Science*. 2014;9.
273. Glisson C, James LR. The cross-level effects of culture and climate in human service teams. *Journal of Organizational Behavior*. 2002;23:767-94.
274. Moore GC, Benbasat I. Development of an instrument to measure the perceptions of adopting an information technology innovation *Information Systems Research*. 1991;2:192-222.
275. CDC. Prevalence and awareness of HIV infection among men who have sex with men --- 21 cities, United States, 2008. 2010/09/25 ed2010. p. 1201-7.
276. CDC. HIV among gay and bisexual men. CDC National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention Division of HIV/AIDS Prevention, 2015.
277. MacKellar DA, Valleroy LA, Secura GM, Behel S, Bingham T, Celentano DD, Koblin BA, Lalota M, McFarland W, Shehan D, Thiede H, Torian LV, Janssen RS. Unrecognized HIV infection, risk behaviors, and perceptions of risk among young men who have sex with men: opportunities for advancing HIV prevention in the third decade of HIV/AIDS. *J Acquir Immune Defic Syndr*. 2005;38:603-14.
278. Mustanski B. Ethical and regulatory issues with conducting sexuality research with LGBT adolescents: a call to action for a scientifically informed approach. *Arch Sex Behav*. 2011;40:673-86; PMCID: Not relevant to NIH public access policy.
279. Mustanski B, Coventry R, Macapagal K, Arbeit MR, Fisher CB. Sexual and gender minority adolescents' views on HIV research participation and parental permission: A mixed-methods study. *Perspect Sex Reprod Health*. 2017;49:111-21, NIHMSID: Journal In Process.
280. Kirk MA, Kelley C, Yankey N, Birken SA, Abadie B, Damschroder L. A systematic review of the use of the Consolidated Framework for Implementation Research. *Implement Sci*. 2016;11:72; PMCID: PMC4869309.
281. Bowen A. Internet sexuality research with rural men who have sex with men: can we recruit and retain them? *J Sex Res*. 2005;42:317-23.
282. Mustanski B. Ethical and Regulatory Issues with Conducting Sexuality Research with LGBT Youth. International Academy of Sex Researchers; San Juan, PR2009.
283. Fisher CB, Arbeit MR, Dumont MS, Macapagal K, Mustanski B. Self-consent for HIV prevention research involving sexual and gender minority youth: Reducing barriers through evidence-based ethics. *Journal of Empirical Research on Human Research Ethics*. 2016;11:3-14.