Research Square

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Title: Keep It Up! 3.0: Study Protocol for a Type III Hybrid Implementation-Effectiveness Cluster-Randomized Trial

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Abstract

Background

Young men who have sex with men are disproportionately impacted by the HIV epidemic in the United States. Few rigorously tested HIV prevention interventions have been developed for young men who have sex with men; previous interventions have primarily focused on in-person programming, with high variability in fidelity. With nearly all young men who have sex with men going online daily, eHealth approaches to prevention may successfully bridge research and practice. Keep It Up! is an eHealth HIV Prevention program for young men who have sex with men. Previous research has demonstrated its effectiveness in reducing sexually transmitted infections and condomless anal sex and efficiency in delivering HIV prevention education. Aim 1 is to compare two strategies for implementing KIU—implementation in community-based organizations and a centralized direct-to-consumer recruitment arm. Aim 2 is to examine adoption characteristics which explain variability in implementation success. Our exploratory aim will develop recommendations and materials for sustainment of KIU after completion of the trial.

Methods

This is a Type III Hybrid Effectiveness-Implementation cluster randomized trial. Using estimates of young men who have sex with men per county in the United States, we identified 113 counties for our sample frame. Using an iterative process, we selected 66 counties to randomize 2:1 to our two strategies in Aim 1. The RE-AIM model for implementation science will be used to drive our outcome measurements in reach, effectiveness, implementation variability, and cost. Outcome measures will be collected from community-based organization staff participants, young men who have sex with men participants, and the technology provider. Our second aim will use mixed-methods research mapped onto the domains of the consolidated framework for implementation research.

Discussion

The trial has launched and is ongoing. This study is among the first to use a cluster randomized trial design in HIV implementation science. In comparing the community-based organization and direct to consumer models for recruitment and ongoing participant engagement, we are examining two strategies which have shown effectiveness in delivering health and technology interventions in the past, but with little base knowledge on their comparative advantages and disadvantages in implementation. The results of the trial will further understanding of the implementation of eHealth prevention interventions.

Trial Registration

NCT03896776, clinicaltrials.gov, 1 April 2019

Contributions To The Literature

- Our trial is among the first to study the implementation of an eHealth HIV prevention intervention.

- Comparing two competing implementation strategies will contribute to knowledge about scaling up future eHealth interventions.
- Our research is among the first to use a cluster-randomized trial for HIV prevention science.
- Identifying clusters for randomization based on the local density of the target population is innovative.

Background

YMSM, HIV, and STIs

Young men who have sex with men (YMSM), ages 18–29, account for nearly 70% of all new HIV diagnoses among adolescents and young adults in the United States,(1) with HIV prevalence estimated at 13.6% in 18–24 year-olds and 18.5% in 25–29 year-olds.(2) HIV infections among YMSM are almost entirely transmitted via unprotected sex,(3–6) defined here as sex with neither Pre-Exposure Prophylaxis (PrEP) nor condoms. Sexually Transmitted Infection (STI) prevalence is also high among YMSM,(7–9) and STIs play an important role in increasing HIV transmission.(10–12) In fact, the Centers for Disease Control and Prevention (CDC) estimates a rectal STI causes a threefold increase in the per-act risk of HIV transmission during receptive anal sex.(13)

Bridging the Research-Practice Divide

Despite increased HIV risk, few interventions in the CDC *Compendium of Evidence-Based Interventions (EBIs) and Best Practices for HIV Prevention Programs*(6) are focused on YMSM.(14) The current arsenal of behavioral EBIs primarily includes face-to-face individual and small-group programs,(6) and their reach has been limited by economic and structural barriers to implementation.(15–20) EBIs have typically been delivered through practice settings such as health departments and community-based organizations (CBO),(21–23) and evidence suggests interventions are not always implemented with fidelity,(15, 16, 24) which can produce a “voltage drop” in effectiveness.(25)

eHealth approaches represent a critical modality for engaging YMSM and delivering intervention content while overcoming barriers to access (e.g., geography(26, 27)) and circumventing delivery challenges (e.g., fidelity(28)). 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.(14, 29–31) Additionally, eHealth has been shown to improve youth access to healthcare services(32) and rates of HIV testing.(33)

The Keep It Up! Intervention

Keep It Up! (KIU) is a web-based, multimedia HIV prevention intervention developed with and for YMSM. Development and efficacy testing of KIU has been extensively described elsewhere.(34–38) In brief, KIU comprises seven modules completed across three sessions with mandatory 8-hour breaks between sessions. Additional content is provided in two booster sessions three and six months after the main intervention. Table 1—Content of the KIU Intervention provides an overview of subject matter covered within each module of the intervention as well as depicts the structured breaks between modules.

Table 1
Content of KIU Intervention

Episode	Module (Have Fun, Stay Safe…)	Main Content
1	In Your Community	Candid interviews with young gay and bisexual men about their communities, family, sex, and relationships that situate these relationships as important aspects of health. Similar interviews on various topics appear throughout the program.
	Hooking Up Online	Three comic book vignettes about meeting men online for sex that focus on identifying factors that may lead to increased HIV risk, such as mood and substance use, as well as preparatory strategies to reduce those risks.
	With Friends	The first chapter of a scripted soap opera that highlights the risks of making assumptions around HIV status and monogamy and promotes positive norms around getting regular HIV testing and utilizing prevention strategies. Remaining chapters appear throughout subsequent modules.
8-hour break		
2	In Bars and Clubs	An interactive game that addresses the consequences of excessive alcohol consumption and drug use, as well as decisional balance around condom use.
	On Dates	An animated story that explores how power dynamics in a dating relationship can affect sexual risk taking. Interactive risk calculators that demonstrate differing levels of HIV and STI risk based on various sexual behaviors.
8-hour break		
3	In Relationships	An interactive animated story and supporting videos that model using good communication skills in relationships to help meet one's sexual, emotional, and health needs.
	In the Future	A goal-setting activity that helps participants identify ways to meet their sexual, emotional, and health needs and troubleshoot obstacles to achieving those goals.
3-month break		
4	Knowing Your Status	New videos and activities that focus on the importance of regular HIV testing in combination with prevention strategies like condoms and PrEP while adding additional layers of nuance, such as sexual pleasure and preventing condom use errors. There is also a check-in on participants' goals.
3-month break		
5	In Love	In addition to checking in on participants' goals, new videos demonstrate when and how to discuss stopping condom use with a partner in a long-term relationship, as well as how to restart condoms after stopping.

KIU has been previously studied in several contexts. A pilot trial among 102 YMSM, ages 18–24, found a significant decrease in condomless anal sex (CAS) compared to a knowledge-based control.(36) A service implementation at a Chicago CBO showed significant pre–post reductions in condom errors, total number of

male sex partners, and CAS among 579 men who have sex with men (MSM), ages 15–24.(34) A multi-city randomized clinical trial with 901 YMSM, ages 18–29, demonstrated a significant 40% decrease in STI incidence as well as a significant decrease in self-reported CAS.(37, 38) Intervention acceptability was high across all three studies, and KIU was subsequently designated a best-evidence HIV prevention intervention by the CDC.(39) KIU is one of the first eHealth HIV interventions with this level of evidence, making it the ideal intervention to study how to scale up.

AIMS

In this manuscript we describe the design of the KIU 3.0 trial, which has the following specific aims:

Aim 1: Compare two implementation strategies using a cluster-randomized trial (CRT). For Strategy 1, CBOs applied for funding to deliver KIU as a service. Strategy 2 is a direct-to-consumer (DTC) model wherein research staff at Northwestern University will recruit participants nationally through online advertising campaigns and manage their engagement.

Aim 2: Examine adoption characteristics that explain variability in implementation outcomes. We will seek to explain variability in implementation success across counties by conducting mixed-methods research(40, 41) on the domains from the consolidated framework for implementation research (CFIR).(42) Data on CFIR characteristics will be collected through administrative data, surveys, and teleconference interviews with key stakeholders.

Exploratory Aim. 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(43) to estimate local impact and costs. We will also examine factors that predict applying for funding and ongoing sustainment.(44) For Strategy 2, we will examine options for ongoing sustainment of the DTC model.

Methods

Cluster-Randomized Trial

Aim 1: Compare two implementation strategies using a CRT.

Sample Frame – County Selection and Randomization

For our sample frame, we selected counties with an estimated number of YMSM greater than 1,500(45) (N = 113 counties). Counties in which KIU has been studied previously were excluded. We randomized 66 counties 2:1 to the CBO and DTC strategies, respectively. Our team opted to randomize 2:1 :: CBO:DTC because we expected that some counties would not have any CBOs apply, or if they applied, some counties' applicant CBOs would not meet minimal requirements for implementing KIU. Further, we randomized 22 counties to receive the KIU DTC strategy because we expected no selection loss(46) from counties where we will advertise online directly to YMSM. KIU will be delivered in each county for two years. Figure 1: KIU! 3.0 Trial Design illustrates our primary design elements. Figure 2 is a CONSORT diagram of the flow of the trial; a

CONSORT checklist was provided as an additional file in submitting this manuscript. See the section entitled *County Selection Iterative Process* in Additional File 1 – Supplemental Information for more details.

Participant Inclusion Criteria and Recruitment

YMSM are eligible for participation in the research components of KIU if they meet the following criteria: 1) test negative for HIV at the time of registration, 2) report that they are assigned male at birth, 3) identify their current gender identity as male or identify as non-binary, 4) are between the ages of 18–29 at registration, 5) report CAS with a male partner in the previous six months, and 6) are not on PrEP, have been on PrEP for less than six months, or report missing a PrEP dose in the previous six months.

Participants will be recruited into KIU using different strategies based on the arm of the study into which they are recruited. For the CBO arm, participants will be recruited at CBO sites after testing negative for HIV. CBO staff will explain KIU and register interested YMSM, who will receive an email with a link that will take them to the application. Once there, participants will complete a baseline survey where their eligibility for the KIU research surveys is verified. In the DTC arm, participants will be recruited primarily through social media, geospatial dating apps, and supplemental approaches (e.g. referrals and print ads). Participants will click through or enter a URL to complete an initial screener for eligibility. When a participant meets all of the other indicators for eligibility, they will be sent an at-home HIV test kit to verify the HIV negative enrollment criterion as well as materials to self-administer swabs and a urine collection cup for oral, urethral, and rectal gonorrhea and chlamydia. See the section entitled *DTC Recruitment* in Additional File 1 – Supplemental Information for additional details on how remote recruitment, screening, and testing will take place in the DTC arm.

Intervention Delivery

KIU 3.0 is a custom mobile, tablet, and desktop responsive web-based application that is developed using multi-tenant architecture. KIU consists of five user roles with separate login pages and varying levels of access to the KIU application: Superusers, Project Directors, Coordinators, Recruiters, and YMSM participants. Superusers are comprised exclusively of Northwestern University project staff who oversee the application's functionality. CBO Project Directors oversee coordinator and recruiter efforts, have access to participant data for intervention retention, and act as primary contacts with KIU project staff at Northwestern University. Non-YMSM user role distinctions are most salient for the CBO arm as DTC project staff functionally have the same level of access as CBO Project Directors. Following completion of the baseline survey, YMSM participants must complete KIU content in sequence, though they are able to return to previously viewed material via a learning map. For more details on intervention delivery, including data collected by the application and the experience of YMSM, see the section entitled *KIU Intervention Delivery* in Additional File 1 – Supplemental Information.

Implementation Strategies - Community-Based Organization Arm – RFP Process

To select CBO recruitment sites, we wrote a request for proposals (RFP) modeled on various RFPs created by CDC and other funders of HIV prevention. Following, we developed an objective scoring rubric and trained objective reviewers to score 3–4 applications on nine criteria. Each application was scored by three distinct

review panelists. Once scores were submitted, we averaged each application's scores and selected the highest scoring applicants for implementation. See the section entitled *RFP Process* in Additional File 1 – Supplemental Information for more details.

Implementation Strategies - Community-Based Organization – Training

Northwestern project staff developed and disseminated online training to CBO implementers. Training modules covered topics ranging from using the implementer dashboard to recruitment strategies. Hosted on the KIU platform, the training includes seamless integration of KIU content. To ensure continuous improvement, Northwestern project staff offer ongoing technical assistance to meet emergent needs of the trial. See the section entitled *Training* in Additional File 1 – Supplemental Information for more details.

Implementation Strategies – Direct to Consumer Arm – Incentives

In the DTC arm, participants will receive a $10 or $25 pre-loaded virtual Visa gift card for completing the first three sessions of the intervention. Incentive amount is randomized by county in order to determine if a threshold amount must be met for incentives to be effective. DTC participants will also receive a discount code for an online store that sells adult toys and products. Participants will be entered into an e-raffle for various prizes donated by vendors as an incentive for completing the booster content at 3- and 6-months post-intervention. This strategy is based on those successfully used by CBO partners in previous KIU service implementations to keep their clients engaged.(34) Participants across both arms of the trial are entered into raffles for $200 gift cards when they complete research surveys at baseline, 3, 6, and 12 months post-intervention.

Measures

The RE-AIM model(47, 48) broadly guided our outcome measurement framework. Aim 1 will use quantitative data on Reach, Effectiveness, and Implementation, while Aim 2 will pull from mixed-methods data on Adoption and qualitative data to explore Maintenance and Sustainability. Outcomes will be measured across four domains: (1) reach to high risk YMSM; (2) effectiveness at reducing HIV risk among engaged YMSM;(47, 49, 50) (3) implementation variability;(51) and (4) cost for delivery.(52, 53) See Table 2: Reach to High Risk YMSM; Table 3: Effectiveness at Reducing HIV Risk among Engaged YMSM; Table 4: Variability in Implementation Success; and Table 5: Cost Elements for a list of outcomes measured by assessment time point.

Table 2
Reach to High Risk YMSM

Level	Construct	Measure/ Operationalization	Measurement Schedule		
			Screening	Baseline	Quarterly
YMSM Participant	Reach	Proportion of YMSM in county screened for KIU	X		
		Proportion of invited YMSM who begin KIU	X	X	
		Proportion of KIU Participants that are Black or Latino		X	
		Proportion of KIU Participants with an STI at enrollment		X	
		Proportion of KIU Participants who engaged in unprotected sex (no condom or PrEP) in prior 6 months		X	
CBO	Reach	Total number of HIV tests conducted		X	X
		Number of HIV tests conducted with YMSM		X	X
		Number of YMSM who tested non-reactive		X	X
		Number of enrolled KIU Participants		X	X
		Number of clients tested for Gonorrhea and/or Chlamydia		X	X
		Number of Gonorrhea and/or Chlamydia tests conducted with YMSM		X	X

Table 3
Effectiveness at Reducing HIV Risk among Engaged YMSM

Outcome Type	Construct	Measure/ Operationalization	Measurement Schedule			
			Baseline	3-month	6-month	12-month
Primary	HIV Risk Behavior	Number of condomless male assigned at birth (MAAB) sex partners	X	X	X	X
		Number of condomless MAAB sex partners who are casual	X	X	X	X
		Risk behavior associated with most recent sexual encounter: condoms, PrEP, substance use	X	X	X	X
	STI Incidence	Urethral and rectal Chlamydia and Gonorrhea - Aptima Combo 2 Assay on the Panther system(1)	X			X
Secondary: Prevention Continuum	HIV/STI Testing	Assessing past 3-month HIV and STI testing history	X	X	X	X
	PrEP Use & Adherence	Current & past 3-month PrEP use; adherence	X	X	X	X
Secondary: Substance Use	Alcohol Problems	AUDIT Alcohol Consumption Questions (AUDIT-C)(2); Full Alcohol Use Disorders Identification Test (AUDIT) branched to those scoring > 3(3)	X	X	X	X
	Other Drug Use	Past 3-month use of marijuana and illicit drugs	X	X	X	X

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Table 4
Variability in Implementation Success

Level	Construct	Measure/ Operationalization	Measurement Schedule				
			Base-line (YMSM) or Pre-Launch (CBO)	3-month (YMSM) or 4-month (CBO)	6-month	12-month	24-month
YMSM Participant	Self-Efficacy	Confidence in HIV testing, condom use, and ability to get on PrEP	X	X	X	X	
	Resource Access	Access to HIV testing, HIV prevention services, and other sexual health services	X	X	X		
	Stigma	Sexual health care avoidance due to LGBTQ stigma	X				
	Satisfaction	Satisfaction with DTC or CBO staff and services	X	X	X		
Technology Center	Engagement	Mean number of KIU modules completed by Participants					
		System analytics; Metrics of activity within modules					
CBO	Demographics		X				
	Effectiveness and Satisfaction with Training	Effectiveness and Satisfaction with Training	X	X			
	Normalization Process Theory	NoMAD: Normalization Process(1)	X	X		X	X
	Organizational Readiness for Change	OCRBS: Organizational Change Recipient Beliefs Scale(2)	X				

Leadership Engagement	ILS: Implementation Leadership Scale(3)	X	X		X	X
Implementation Climate	ICS: Implementation Climate Scale(4)	X			X	X
Readiness for eHealth	Readiness for eHealth (Developed from cited sources)(5–7)	X				
Sustainability	Program Sustainability Assessment Tool(8)				X	X
Adaptation	Items based on the Frame measure(9)				X	X
CFIR domains	Administrative Data	X	X	X	X	X
	Qualitative Interviews	X			X	

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Table 5
Cost Elements

Cost Type	Construct	Measures	Source	Measurement Schedule
Start-Up	Recruitment	Staff time, consultant and other costs	Staff activity logs; study records and CBO interviews/surveys	Monthly for start-up period; one-time
	Initial Training	Number and duration of trainings	Study records	One-time
	Technology development	Staff time, content development costs	Staff activity logs	Monthly for start-up period; one-time
Variable	Shipping and processing HIV and STI test kits	Number of units shipped, STI lab cost per test, staff time per shipment	Study records; staff interviews	Ongoing; one-time
	Participant contacts	Number of Participant contacts, staff time per contact	Participant contact logs; staff interviews	Ongoing; one-time
Time-Dependent	Social Media Advertisement	Total spending	Study records	Ongoing
	Booster Training and Technical Assistance	Staff time by arm	CBO and DTC Participant tracking logs; staff activity logs	Ongoing; monthly
	Other staff activities	Staff time by arm	Staff activity logs; CBO interviews/surveys	Monthly; one-time
	Space and occupancy costs	Square feet	Staff interviews	One-time

Data Analysis – Public Health Impact

Our primary outcomes are public health impact (PHI), defined as reach X effectiveness(47, 49, 50), and cost per infection averted.(54, 55) For this trial, PHI will be assessed by (1) reach into the county's YMSM community, weighted by HIV risk, and (2) effectiveness at reducing HIV risk.(47, 49, 50) By measuring individual-level change on these modifiable factors, our index of PHI will allow for heterogeneity in response to KIU across individuals, race and age groups, counties, and implementation condition. Effectiveness will be marked by the estimated change in that person's risk for HIV from baseline to follow-up surveys, determined by observed changes in target risk behavior: CAS, STIs, and adherent PrEP use, all of which have major impacts on HIV transmission in MSM.(56–58) We will base our modeling of HIV risk on published single-exposure probabilities and account for multiple exposures using binomial modeling.(59) Because these are individual-based measures, we will use two-level mixed-effect modeling.(60) 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.(54, 55)

We will follow established guidelines for collecting cost data and conducting economic evaluations and will conduct cost analyses for each arm from the perspective of the healthcare sector.(52, 53) We will follow a 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.

Data Analysis – Compare CBO and DTC Implementation Strategies

We will employ Multivariable Generalized Linear Mixed Models (GLMM) for our analyses, as they account for nested individual observations within counties and are commonly used in CRTs.(53, 61) The multivariable aspect of the model will allow for the control of factors that are unbalanced between arms either because they were not accounted for in the randomization process or because they may have become unbalanced due to loss to follow-up. To account for potential selection bias in constructing an efficient (1 degree of freedom) 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.(46, 62) Similar to propensity score analysis, we will also formally include the model that predicts selection effects.(63) We will estimate standard errors using nonparametric bootstrapping techniques within the multivariable framework treating arm as a dichotomous indicator.(53) 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-effectiveness analysis, parameters obtained from bootstrapping will be used to estimate cost-effectiveness acceptability curves which will indicate the probability that either intervention is a good value for different willingness-to-pay thresholds (i.e., incremental cost per infection avoided).(64) 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.(65–67)

Study Status

The KIU trial commenced in October 2019. As of October 2020, the DTC arm has begun recruitment in all 22 of its counties. The CBO arm has launched 20 counties for recruitment; the remaining two sites will initiate their programs in fall 2020. The CBO arm has gathered both qualitative and quantitative baseline data on implementation from 20 CBOs. See the section entitled *CBO and DTC Study Statuses* in Additional File 1 – Supplemental Information for additional details on study status for each arm.

Discussion

A large CRT is innovative in HIV research. There has been a recent increase in their use in public health and medicine,(68) but with a few important exceptions,(69–72) they have not seen significant application in HIV

implementation science. Our design of systematically selecting counties with large YMSM populations and then randomizing them to an implementation strategy is innovative. Particularly innovative is our strategy to solicit RFPs 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.

Our trial compares the implementation of two competing implementation strategies – CBO vs DTC. Both are viable strategies for eHealth intervention dissemination. The CBO model, with CBOs directly funded by the CDC or their local health department,(73) is the current backbone of implementing HIV prevention programs. The DTC model introduces a novel method of mitigating barriers to regular HIV/STI testing(74–78) by facilitating self-testing, which has been demonstrated to be accurate, acceptable, and feasible, especially among those who may not otherwise seek an HIV test.(79–85) While both the CBO and DTC arms 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(51, 86) that could help boost and shape future dissemination and implementation of eHealth HIV prevention interventions(87, 88) and contribute to greater scalability, reach, and public health impact.

Our trial will contribute to implementation science, with a particular focus on eHealth. Effective implementation has been described as the greatest challenge to HIV prevention,(89) 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.(15, 16, 20) While prior implementation science has compared capacity-building approaches for individual and small-group prevention programs,(24, 90–92) there has been little-to-none on eHealth HIV prevention.(30, 31, 93, 94) 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.(95)

Abbreviations

Term	Acronym
Centers for Disease Control and Prevention	CDC
Cluster-Randomized Trial	CRT
Community-Based Organization	CBO
Condomless Anal Sex	CAS
Consolidated Framework for Implementation Research	CFIR
Direct-to-Consumer	DTC
Evidence-Based Intervention	EBI
Food and Drug Administration	FDA
Human Immunodeficiency Virus	HIV
Keep It Up!	KIU
Male Assigned At Birth	MAAB
Men Who Have Sex With Men	MSM
Multivariable Generalized Linear Mixed Models	GLMM
National Institutes of Health	NIH
Pre-Exposure Prophylaxis	PrEP
Public Health Impact	PHI
Randomized-Controlled Trials	RCTs
Request for Proposals	RFP
Research Electronic Data Capture	REDCap
Sexually Transmitted Infection	STI
Short Message Service	SMS
U.S. Food and Drug Administration	FDA
Young Men Who Have Sex With Men	YMSM

Declarations

Ethics Approval and Consent to Participate

This protocol was approved by the IRB at Northwestern University, IRB reference number STU00207476. The protocol is currently on version 1.9. YMSM and CBO staff participants will be informed of the aims of the study as well as data protection; all participants will be consented to participate in our trial. Reports derived from our trial will be delivered in aggregate such that participants cannot be identified.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets generated and/or analyzed during this trial will be available from the investigators upon reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

BM is the principal investigator of the trial, and led the design of the study, the research team, and data collection; he participated in the writing and editing of the manuscript. JPJ wrote the abstract and sections on the county selection and RFP processes, CBO study status, and discussion; he also acted as project lead in constructing the manuscript and provided substantial editorial support across all sections. NB provided content and editorial support for the RFP process and CBO study status and contributed to the design of the study. KM and KLM co-wrote all DTC sections; KM contributed to the design of the study. GS and EB co-wrote the sections on participant inclusion criteria, measures, and data analysis as well as constructed measures tables. BRS and AS contributed content and editorial support to the data analysis and measures tables; BRS contributed to the design of the study. DHL and RS co-wrote the sections on the KIU intervention background and intervention delivery. JDS and CHB contributed to the design of the study and provided editorial support for the data analysis and measures sections of the manuscript. AD wrote the section on CBO training. BPL and PJ contributed to the design of the study. All authors read and approved the final manuscript.

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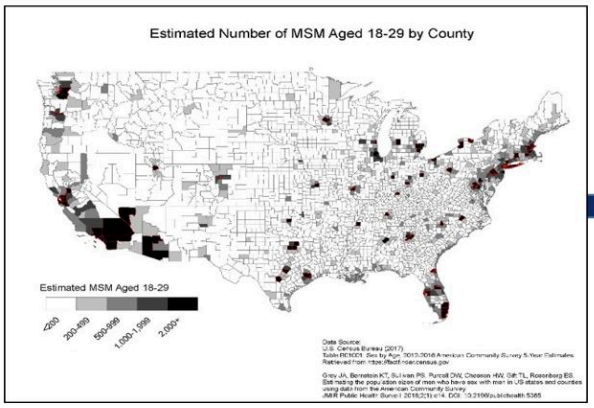
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Figures



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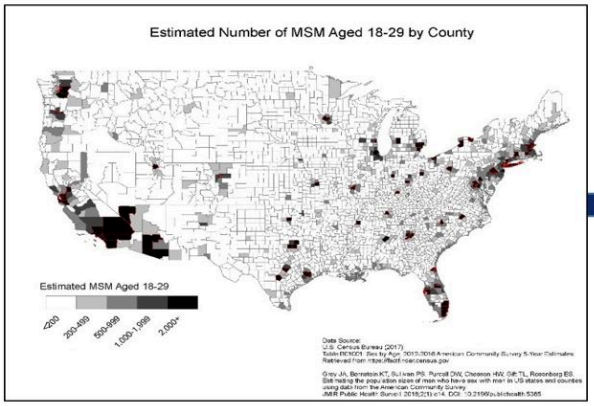
Identify counties with >1,500 YMSM (N=113)	
Iterative process to identify 66 counties for sample frame	
66 counties randomized→2:1	
44 counties randomized to CBO strategy	22 counties randomized to DTC strategy

Request for proposals from CBOs in 44 counties	
Applications received, reviewed, and scored.	
22 top scoring applications (1 per county) funded	
Customization of CBO KIU instances	
CBO staff deliver KIU to YMSM who test HIV negative through their routine HIV testing programs. STI testing provided through CBO or remotely. CBOs receive ongoing coaching from NU project staff.	
CBO staff engage YMSM in KIU	Research staff assure survey completion
12 month STI testing performed at CBO or through remote testing	

Advertising campaign designed and launched for 22 counties.	
At least 100 YMSM are recruited in each county.	
Eligible YMSM receive kit through the mail for HIV/STI self-testing.	
KIU engagement by NU DTC staff.	Research staff assure survey completion.
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Figure 1

KIU! 3.0 Trial Design illustrates our primary design elements.



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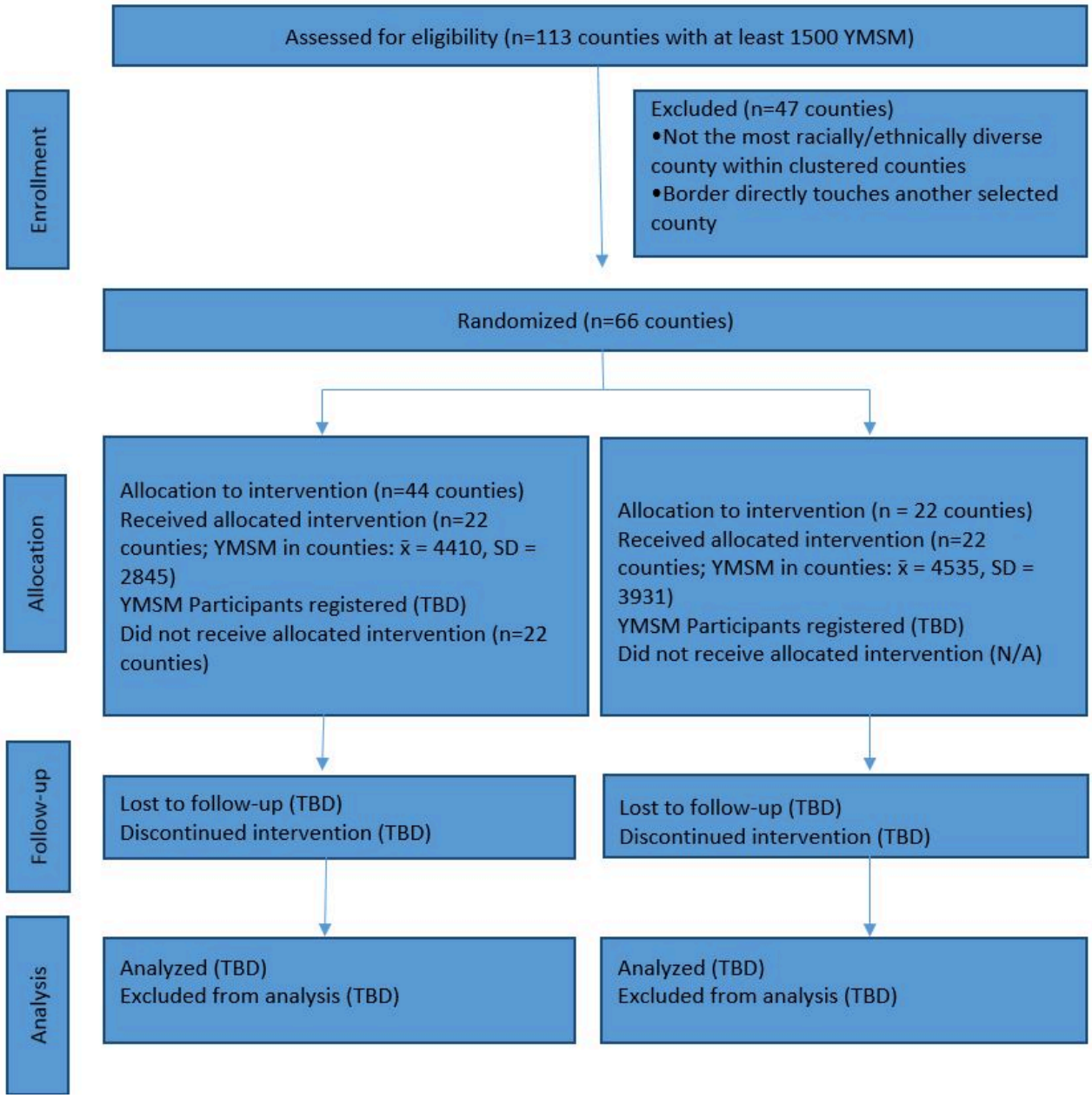


Figure 2

CONSORT diagram of the flow of the trial

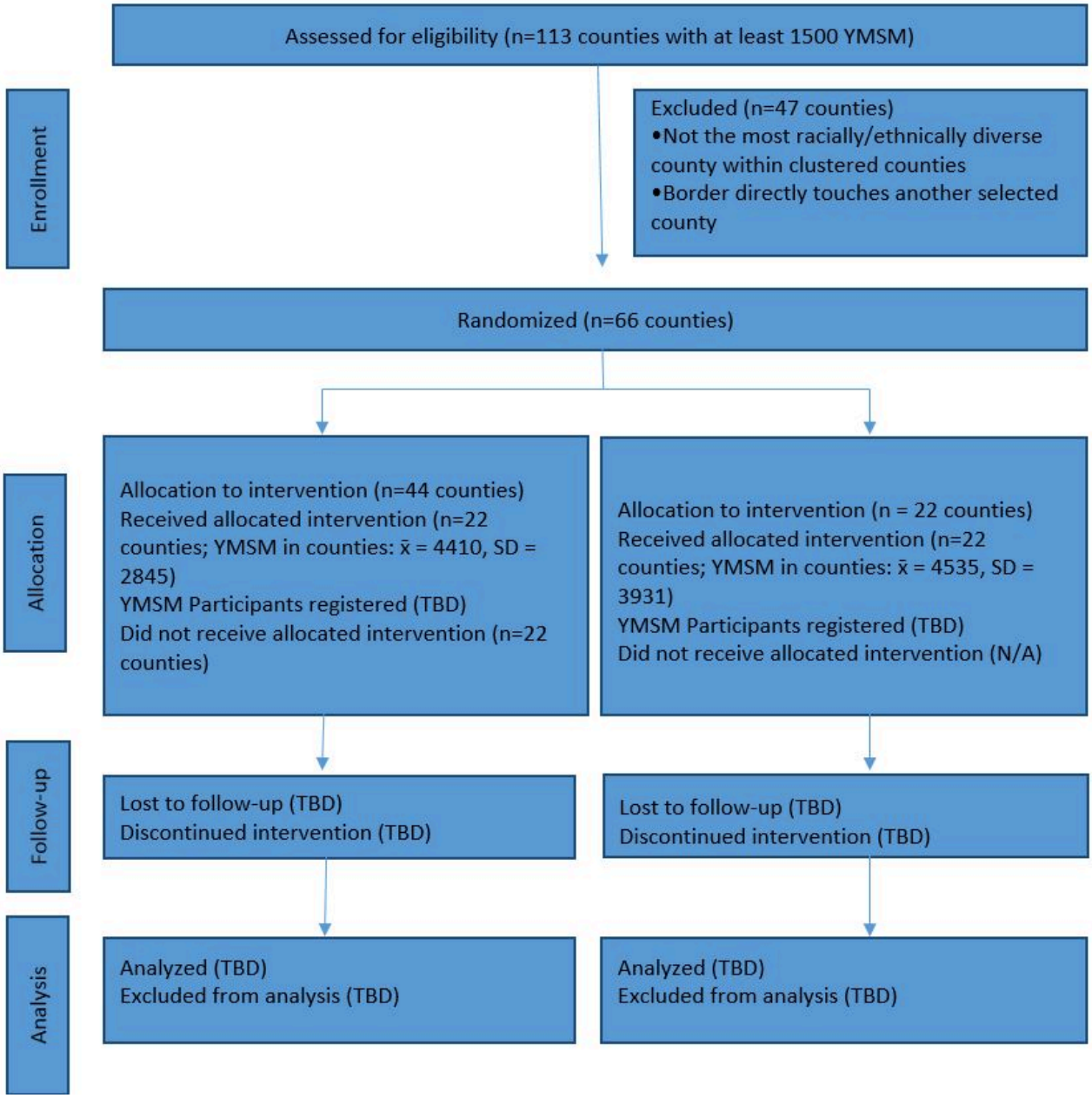


Figure 2

CONSORT diagram of the flow of the trial

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFile1SupplementalInformationtablemoved.docx
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- KIU3.0Protocolv.1.98September2020clean.docx

- KIUProtocolPaperCONSORTChecklist.docx
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