TITLE OF RESEARCH STUDY: A MULTIDIMENSIONAL DIGITAL APPROACH TO ADDRESS VACCINE HESITANCY AND INCREASE COVID-19 VACCINE UPTAKE AMONG AFRICAN AMERICAN YOUNG ADULTS IN THE SOUTH (TOUGH TALKS COVID)

NCT05490329

DOCUMENT DATE: 07APR2023LATE PROTOCOL

PROTOCOL TITLE:

A Multidimensional Digital Approach to Address Vaccine Hesitancy and Increase COVID-19 Vaccine Uptake among African American Young Adults in the South (Tough Talks COVID)

PRINCIPAL INVESTIGATORS:

Lisa Hightow-Weidman, MD MPH
College of Nursing
Phone: 850-644-5260
E-mail: lhightowweidman@fsu.edu

Henna Budhwani, PhD MPH
College of Nursing
Phone: 850-644-5260
Email: hbudhwani@fsu.edu

VERSION NUMBER/DATE:

Modified from UNC Version 3.0 08/02/2022

FSU Version 1.1 01/06/2023

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
1	01/06/2023	Update randomization schema to include balanced assignment within given study states	N

Table of Contents

1.0 Study Summary

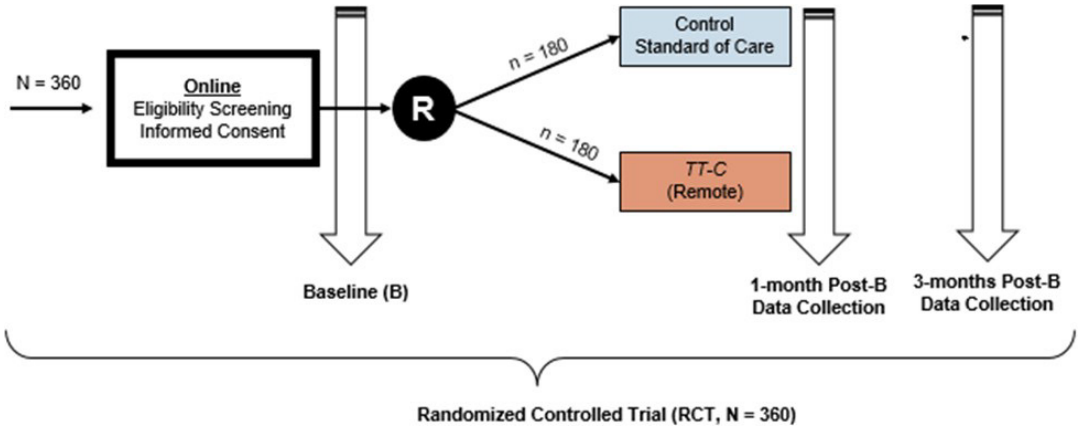
Study Title	A Multidimensional Digital Approach to Address Vaccine Hesitancy and Increase COVID-19 Vaccine Uptake among African American Young Adults in the South (Tough Talks COVID)
Study Design	Hybrid type 1 effectiveness implementation 2-arm RCT with 360 AA-YA from AL, NC, and GA
Primary Objective	The overall objective of the research study is to adapt and test the efficacy of the Tough Talks-COVID (TT-C) app among 360 AA-YA ages 18-29 recruited from community partners in AL, GA, and NC. The primary outcome is COVID vaccine uptake and series completion.
Secondary Objective(s)	Secondary outcomes are VH, confidence, and knowledge, attitudes, and beliefs.
Research Intervention(s)/ Investigational Agent(s)	Tough Talks COVID (TT-C) Mobile Application
IND/IDE # (see section 5)	N/A
Study Population	Aim 1 (online survey and DST workshops) (complete): 1) YA aged 18-29 2) identify as AA 3) English proficient 4) access to a personal smartphone 5) current resident of AL, GA or NC. Aim 2 (focus group) (complete): 1) YA aged 18-29 2) identify as AA 3) English proficient 4) access to a personal smartphone 5) express COVID vaccine hesitancy (VH) 6) reside in one of the six intervention communities in AL, GA, and NC. Aim 3 (2-arm randomized controlled trial): 1) YA aged 18-29 2) identify as AA 3) English proficient 4) access to a personal smartphone 5) express COVID vaccine hesitancy (VH) 6) reside in AL, GA, and NC

	Not eligible: having received full series of COVID vaccine doses (including vaccines plus booster or prior participation in a vaccine trial).
Sample Size	Total study sample is ~544 of which the following will be enrolled for each aim: 1) online survey with 150 participants; up to 24 of whom will be selected to participate in the DST workshops; 2) focus groups with up to 16 participants, beta testing with community and YAB members; 3) 2-arm RCT conducted with 360 participants. The TT-C remote and standard of care arms will each include 180 participants.
Study Duration for individual participants	Study duration for participants in Aim 1 is up to four weeks for those participating in the DST workshops. Study duration for participants in Aim 2 is up to 2 months. The duration of study for RCT participants is 3 months.
Study Specific Abbreviations/ Definitions	AA African American AA-YA African American Young Adults ACTG AIDS Clinical Trials Group ACASI Audio Computer Assisted Self Interview AE Adverse Events AES Advanced Encryption Standard AIDS Acquired Immunodeficiency Syndrome AL Alabama ATN Adolescent Medicine Trials Network for HIV/AIDS Interventions CASI Computer assisted self-interview CBPR Community Based Participatory Research CDC Center for Disease Control and Prevention CFR Code of Federal Regulations CoC Certificate of Confidentiality COVID SARS-CoV-2 CRF Case Report Form CYOA Choose Your Own Adventure DHHS U.S. Department of Health and Human Services DHIs Digital Health Interventions DSW Digital Storytelling Workshop E2E End-to-End EC Ethics Committee EUA Emergency Use Authorization FISMA Federal Information Security Management Act FIPS Federal Information Processing Standards GA Georgia GCP Good Clinical Practices HBCU Historically Black Colleges and Universities

	HIPAA Health Insurance Portability and Accountability Act HITECH Health Information Technology for Economic and Clinical Health Act HIV Human Immunodeficiency Virus ICH International Conference on Harmonization IRB Institutional Review Board NC North Carolina NICHD National Institute of Child Health and Development NIDA National Institute on Drug Abuse NIH National Institutes of Health NIMHD National Institute on Minority Health and Health Disparities PI Principal Investigator OHRP Office of Human Research Protection QNS Query and Notification System RCT Randomized Control Trial RDC Remote data capture RDS Respondent-Driven Sampling SAGE Strategic Advisory Group of Experts SID Study ID Number SOC Standard of Care SSAE Standards for Attestation Engagements SSL Secure Sockets Layer TLS Transport Layer Security TT-C Tough Talks COVID UNC University of North Carolina UPiRSO Unanticipated Problem involving Risk to Subjects or Others VH Vaccine Hesitancy YA Young Adults YAB Youth Advisory Board

PROTOCOL TITLE: A Multidimensional Digital Approach to Address Vaccine Hesitancy and Increase COVID-19 Vaccine Uptake among African American Young Adults in the South (Tough Talks COVID)

RCT Schema:



2.0 Objectives

2.1 The overall objective of the research study is to adapt and test the efficacy of the Tough Talks-COVID (TT-C) app among 360 AA-YA ages 18-29 recruited from community partners in AL, GA, and NC. The primary outcome is COVID vaccine uptake and series completion.

Secondary outcomes are VH, confidence, and knowledge, attitudes, and beliefs.

2.2 We hypothesize that the intervention arm will be more effective than the control arm at increasing vaccine uptake

3.0 Background

3.1 Young Adults (YA) are a key "super-spreader" population transmitting SARS-Co-V2, the causative agent of COVID-19 (COVID). Interventions to increase the uptake of COVID vaccination among YA are central to ending the pandemic.[1] Given their high rate of asymptomatic infection[2] compounded by transmission rates that are being fueled by behaviors that run contrary to physical distancing and face covering regulations, YA represent a priority population upon which to focus efforts to ensure high levels of COVID vaccine uptake.[1] Indeed across the Southern US, increases in positive SARS-CoV-2 test results among YA were found to precede increases among older adults (aged ≥60 years) by 4–15 days, providing evidence for the significant contribution YA play in sustaining community transmission.[3] YA have been implicated in local COVID outbreaks and infection clusters[4] linked to bars,[5] parties[6,7] and college campuses.[8] High rates of employment in public facing essential jobs often do not allow YA to work remotely.[9,10] Further, YA who identify as African American (AA-YA) often have the social capital to influence health behaviors in older family and community members who are at high risk for COVID morbidity and mortality.[11]

Digital Health Interventions (DHIs) can reach large numbers of YA regardless of geographic location and empower them to make informed decisions about their health using a familiar modality that YAs value and trust. Our collaborative team developed the theory informed DHI Tough Talks to assist YA with HIV disclosure decision making, specifically by considering the social, ethical and behavioral implications of their choices and the consequences that follow. In response to NOT-MD-21-008: Research to Address Vaccine Hesitancy, Uptake, and Implementation among Populations that Experience Health Disparities, we propose to leverage lessons learned from the HIV epidemic among YA and AA-YA and apply a

community-based participatory research (CBPR) approach to adapt and test Tough Talks to address COVID vaccine hesitancy, Tough Talks-COVID (TT-C).[12] Our CBPR approaches are grounded in equitable communities partnerships, and strive to be mutually beneficial throughout the life of a project, from inception to dissemination. Attention to equity is critical for research within AA communities, who face a legacy of misrepresentation, discrimination, and exploitation in clinical research which has engendered understandable mistrust of vaccines, medicine, and research.[13]

The TT-C intervention will enable AA-YA to actively make autonomous decisions about COVID vaccine receipt using non-stigmatizing and YA-tailored messaging. Through engaging activities and narrative communication, TT-C will address the structural contexts (e.g. emotionally charged, issues of confidence and distrust in medicine, stigma), mis-information (e.g. vaccination knowledge), environmental barriers (e.g., access to care, health insurance) and potential consequences (e.g. outcomes related to accepting or refusing vaccination).[14] Using CBPR methods to co-create TT-C with AA-YA will promote personal agency, bolster resilience in the face of the pandemic, strengthen intervention quality, and increase intervention relevance and engagement.[15-17] We will employ CBPR methods to assess multi-level factors identified within the NIMHD Research Framework at the individual (knowledge, attitudes, and normative beliefs), interpersonal (peer and family influence), institutional (provider communication, health care system) and structural level (stigma, discrimination) that influence COVID vaccine hesitancy (VH) and refusal. We will leverage novel data collection methods to reach and engage AA-YA through the conduct of our multiphase, implementation science randomized controlled trial (RCT).

3.2 Vaccine Hesitancy (VH) is complex, influenced by factors at the individual, community, provider, health care system, and societal levels.[20] A cross-sectional online survey of US adults (n=2,650) conducted in December 2020 found that respondents who reported experiences of racial discrimination had 21% increased odds of higher VH compared to those who did not report such experience.[21] Thus, as espoused by the WHO Strategic Advisory Group of Experts (SAGE), individual/social group influences, contextual influences, and vaccine-specific issues must be identified and then targeted through multi-component and tailored interventions to increase vaccine uptake within relevant populations.[22] We therefore utilize the NIMHD Research Framework, informed by the SAGE Working Group (Figure 1) to provide a model for depicting the determinants

relevant to understanding and addressing VH in AA-YA and to guide our intervention development.[23]

Building capacity and promoting AA-YA agency through co-creation of the intervention will foster resilience in the face of the pandemic, strengthen intervention quality, and increase engagement with intervention content.[15-17,24] COVID has exacerbated disparities experienced by AA-YA, particularly those residing in the underserved US South. AA face significantly more morbidity than other races. From May-August 2020 Black individuals accounted for 18.7% of overall deaths despite making up just 12.5% of the US population.[25] COVID continues to disrupt economic resources, social networks, and healthcare services[26] across socioecological levels, disproportionately affecting disparity populations such as AA-YA.[27] Stigma, discrimination, and distress due to COVID are widely evident,[28] and highest among those with intersectional identities (e.g., AA, YA, rural, etc.),[29] reinforcing health inequities.[30,31] Comprehensive multi-component interventions, situated in the existing contexts of racial disparities and discrimination, that are responsive to the diverse needs of AA-YA, and address both the structural and psychosocial barriers to COVID vaccination are critically needed. To this end, our project is rooted in community-based participatory research (CBPR) methods as an innovative way to partner with communities most impacted by the pandemic.[12,32-34] Our approach explicitly engages with the social and ethical implications of research with AA communities, who face a history of misrepresentation, discrimination, and exploitation which has engendered valid and understandable mistrust of medicine and research.[13]

Digital Health Interventions (DHIs) are well-suited for YA given the ubiquity of technology use and their suitability for delivering content tailored to each user's unique needs. DHIs can increase knowledge, self-efficacy, and motivation for behavior change while ameliorating distrust, fear, and stigma across a variety of health conditions.[35-40] YA already rely on digital technologies to build their social networks, receive social support, and obtain health information.[37,41,42] Access to credible online resources is critical given the majority of YA access COVID information from online news and social media sites.[43] Likewise, misinformation via social media can increase behaviors that perpetuate COVID VH.[44] Our team in on the forefront of designing stand-alone, preventative health DHIs that hold promise for engaging AA-YA to address COVID VH and uptake.[37,45-49] Specifically, the Tough Talks DHI (R43/R44 MH104102) was developed to assist youth living with HIV with disclosure decision making by considering the social, ethical and

behavioral implications of their choices and the consequences that follow.[50-52] Tough Talks was informed by Social Cognitive Theory (SCT); the inclusion of emotionally engaging scenarios, interactivity, and automation promotes observational learning, social modeling, and reinforcement of behavioral skills (Figure 2). Feasibility and acceptability of the platform for AA-YA males has been established; early results from a national RCT appear promising for impacting disclosure decisions (see Section C.5). For these reasons, we have chosen to adapt Tough Talks, a culturally tailored and theoretically informed DHI to increase COVID vaccine uptake in stigmatized AA-YA in three southern states.

3.3 Acceptance of COVID vaccination is lowest among YA and African Americans (AA). Two highly effective vaccines for COVID were given Emergency Use Authorization (EUA) by the FDA in December, the Moderna and Pfizer, mRNA vaccines. The Moderna vaccine showed 94% and Pfizer 90% efficacy in phase 3 trials. Both vaccines require 2 doses about 3-4 weeks apart. Despite the high efficacy, the rapid development and testing of these vaccines has resulted in public concern around safety of the vaccines. This built on a history of medical mistrust has result in low levels of willingness to take up a vaccine in surveys done among AA populations in the US. Rates of COVID-19 vaccination are currently at 61.8% in Alabama, 64.3% in Georgia, and 82.2% in North Carolina, with rates continuing to be lower among African American populations in southern states. A recent 2022 Health Resources and Services Administration (HRSA) report found that only 54.5% of African American residents in surveyed Georgia clinics accepted their first vaccine dose, 10% lower than the overall state rate and only 34.1%, 34.9%, and 25.1% of Alabama, Georgia, and North Carolina residents, respectively, have accepted a booster. Those who remain unvaccinated may be highly resistant toward accepting vaccination or are overwhelmingly apathetic. Further, lower vaccine acceptance was associated with younger age (18-49 years) in a nationally representative survey conducted in October 2020 among US residents (n=525).[19]

All aims of this study have been previously reviewed and approved by the University of North Carolina at Chapel Hill IRB. Aims 1 and 2 were completed while the research team was at UNC-CH. By submitting this protocol to Florida State University, we are seeking IRB approval for the RCT (Aim 3) and analysis activities only. The original protocol, study documents, and approval letters are appended in the IRB submission.

4.0 Study Endpoints

4.1 The primary study endpoint is COVID vaccine uptake and series completion. The secondary study endpoint is change in vaccine hesitancy, vaccine confidence, and change in knowledge, attitudes, and beliefs.

4.2 N/A

5.0 Investigational Test Articles or Products

5.1 The Tough Talks COVID intervention is a mobile app co-created with AA-YA using CBPR methods. The application enables AA-YA to actively make autonomous decisions about COVID vaccine receipt using non-stigmatizing and YA-tailored messaging. It includes engaging activities and narrative communication, and seeks to address structural contexts, misinformation, environmental barriers, and potential consequences.

5.2 N/A

5.3 N/A

5.4 N/A

6.0 Procedures Involved

6.1 This study will consist of three distinct aims to develop and test the TT-C intervention for COVID vaccine hesitant AA-YA. Aims 2 and 3 procedures are premised on the formative data collected in Aim 1.

Aim 3: Conduct a hybrid type 1 effectiveness implementation 2-arm randomized controlled trial with 360 AA-YA from AL, NC, and GA.

6.2 Enrollment: After screening eligible and agreeing to be contacted, eligible responses will be reviewed individually by study staff to determine authenticity and legitimacy. In addition to eligibility criteria, staff will review bot detection values as well as location based on IP address & latitude/longitude. If determined eligible, staff complete the Verification CRF and REDCap will email the individual with a unique consent form link to complete. Once completed, REDCap will send the baseline survey linked to their unique ID in REDCap.

After the baseline survey is complete, study staff will randomize the participant with the Randomization CRF to either the intervention or control group. Based on the study arm, study staff will either email the participant with the developed SOC materials or email the participant with a unique link to create their account for the TT-C app. If SOC, the participant will be compensated at this time.

If participant is randomized to intervention arm, they will be prompted to create their account with the provided link, then will be

directed to download and login to the TT-C app. Once account creation is confirmed in the administrator portal, study staff will compensate the participant for enrolling.

Randomization: RCT participants will be randomized via block randomization into the control condition and TT-C (remote), each with a balanced 180 participants. Assignment will be stratified by state to achieve balance between intervention and control participants within a given study state.

Locator/Contact Information Collection: Once consented and enrolled, designated site study staff will collect contact information from the participant. Participants will be asked to provide contact information through which they can be reached. Participants will also be asked to provide valid contact information for two family members and/or friends who can be called in the event the participant cannot be reached by phone or email. Participants will be asked if messages can be left at the numbers provided. Study staff will not leave messages unless expressly permitted to do so by the participant which also will be documented. If permission is given to leave messages, site staff will assure participants that messages left with a family member or friend will only ask the participant to contact study staff and will not include any protected health information or information related to study participation.

The Contact Information Worksheet will not contain any study data and will be maintained under double locks at the study site, separate from all study records, with access limited to designated site research personnel.

Optional Monkeypox Module: Participants will also be given the opportunity to complete an optional set of questions about Monkeypox immediately following the baseline survey.

TT-C arm: Once enrolled, participants will be emailed a unique link to create their TT-C account and instructions on how to download the TT-C (remote) app from the iOS or Google Play store. They will be asked to complete the intervention within one month. Participants will be compensated for completing the baseline survey and reminded that they will be asked to return (virtually) in 1 and 3 months for follow-up.

Standard of Care arm: Research staff will provide COVID vaccine materials from the CDC to those participants in the SOC arm. Participants will be compensated for completing the baseline survey and reminded that they will be asked to complete 1 and 3-month follow-up surveys. To provide the maximum benefit through this trial, after the completion of the data collection associated with the

primary RCT, those randomized to the control arm who still report VH will be offered the opportunity to accept the TT-C intervention delivered remotely. These participants will be asked to use the app for one month and complete follow-up surveys at their 4- and 6-month time points (same surveys used for 1 and 3M). These participants will be compensated for survey completion.

Participants will also be asked to complete exit interviews to discuss their experience with the intervention and/or their knowledge, attitudes, and perceptions of COVID-19 vaccination.

6.3 Research Staff Training: All proposed study staff have participated in the required trainings in participation and conduct of studies that involve human subjects, and any future study staff will do so upon hiring. Training for all research staff includes (but is not limited to): an overview of the study; study procedures and human subjects issues (informed consent process, confidentiality); a demonstration of all technology components; methods for establishing comfort with the sensitive issues that may arise in the course of the focus groups or assessments; Human Subjects Protection; Good Clinical Practice; informed consent; quality management; confidentiality; and reporting of adverse events.

Intervention Monitoring/Quality Control: Because the TT-C intervention is an app, intervention fidelity is assured for all activities except for the reflection activities and facilitation of vaccination appointments.

Data Platform Security: We use SSL encryption for transfers of information online and data will be stored in the secure, HIPAA-compliant servers of the Florida State University. The CASI data will be stored in a secure database at Qualtrics and REDCap.

Qualtrics and REDCap use Transport Layer Security (TLS) encryption (also known as Hypertext Transfer Protocol Secure (HTTPS)) for all transmitted data. Survey data are protected with passwords and HTTPS referrer checking. The data is hosted by third party data centers that are Statement on Standards for Attestation Engagements (SSAE)-16 Service Organization Control (SOC) II certified. All data at rest are encrypted, and data on deprecated hard drives are destroyed by U.S. Department of Defense methods and delivered to a third-party data destruction service.

Qualtrics and REDCap deploy the general requirements set forth by many Federal Acts including the Federal Information Security Management Act (FISMA) of 2002. They meet or exceed the minimum requirements as outlined in Federal Information Processing Standards (FIPS) Publication 200.

Health Insurance Portability and Accountability Act (HIPAA) Statement: With some restrictions, Qualtrics and REDCap may be designated as Business Associates when the Qualtrics and REDCap BA Agreements are signed with a Covered Entity—those organizations that are required to comply with HIPAA privacy rules. All client data are considered confidential and treated as such.

Related to HIPAA, Health Information Technology for Economic and Clinical Health Act (HITECH) are updated assessment rules to ensure that data are properly protected and best security practices are followed. By using secure and certified data centers, Qualtrics and REDCap ensure the highest protection and testing as per HITECH requirements.

Zoom Platform Description: The Zoom platform may be used to conduct qualitative interviews remotely. Participants will have the option to conduct face-to-face video chat, video chat in which they can see the interviewer, but the interviewer cannot see them, or audio chat only. Zoom is compatible on PCs, tablets, and smartphones; as well as maintains the option to conduct an audio conference without the video component. Zoom offers HIPAA-compliant versions of its platform. Study staff will use HIPAA-compliant version of Zoom for study activities.

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

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

scalable and highly available meeting infrastructure unrestricted by the limitations of physical data centers.

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

The Zoom sessions will contain identifying information, as in VSee above, but this information will be stripped form the recorded Zoom sessions before they are sent to the analysis team for content analysis.

Back Up Recording: All qualitative interviews may also be recorded using a back-up digital audio recorder. Audio files will be erased after being transcribed and transcripts will be de-identified. All audio files will be kept confidential and stored in a locked/limited access folder on secured servers, which is only accessible to designated study staff. All members of the research team will be trained in confidentiality and have signed confidentiality agreements. A professional transcription service, experienced in the handling of confidential data, will be used to fully transcribe verbatim all audio files. Prior to receipt of the first audio file, the transcription service will be instructed to exclude from the typed transcript identifying information (e.g., a name) that may have been verbalized during the course of the interviews.

6.4 The study team is responsible for the development of this protocol as well as the Case Report Forms (CRFs) needed to collect the information required to implement this protocol.

Data Records: Participant-related study information will be identified through a study ID number (SID) and participant code on all participant CRFs, audio files, transcripts, and CASI files. Participant names or other personally-identifying information will not be used on any study documents other than the Contact Information Worksheet (if used, stored in double-locked office separate from other study information only accessible by designated study staff) and will be redacted from focus group and exit interview transcripts. All study-related information will be kept in double-locked, limited access areas at each study site. Participant names and their SID and participant code will be stored in separate tabs in REDCap, accessible only to designated study staff, site monitors, and representatives from the NICHD. SIDs will not be entered into the mobile app and instead a unique app ID will be assigned to each participant and used when logging into the app. These unique App IDs will be provided by the developer and recorded into REDCap

during enrollment. Original source documents (e.g., Contact Information Worksheet) for individual participants will be maintained at the respective site and will be accessible only to the study staff. Data from original source documents will be transcribed on CRFs as applicable. Electronic data will be stored in Box, OneDrive or on a secure server at FSU.

Audio-Recorded Data: Audio recorded data from the focus group sessions will initially be stored as a digital file on a secure encrypted FSU server. Focus groups will be transcribed verbatim from the digital audio recording and de-identified by assigning unique numerical codes. After transcripts are verified by the research team and one year after the study is over, audio files will be destroyed.

CRFs: Study monitoring data, including information about eligibility, demographic data and monitoring untoward effects, will be collected on CRFs. All CRFs for this study must be entered into REDCap. Hard copies will be made available for download from a FSU-run secure cloud management platform, to be used if needed.

CASI Survey Data: Data collected using a CASI method at the community partner sites will be entered on a portable computer or mobile phone via an internet-based application. All data collected using CASI will remain confidential; no personally identifying information will be collected during the computer session. The participant's unique SID number will be used in order to link the participant to the responses.

CASI Data Security: Only authorized users with a login name and password will be able to access and open the online HIPAA-compliant online CASI platform administered survey.

6.5 N/A

6.6 N/A

7.0 Data and Specimen Banking

7.1 N/A

7.2 N/A

7.3 N/A

8.0 Sharing of Results with Subjects

8.1 After completion of analyses, overall study results will be shared with participants in the form of a lay summary and/or infographic. This information will be sent to participants via the email they consented to using for study purposes.

Any manuscripts for academic publication or other publicly available materials generated as a result of this work will not individually identify participants in this study.

9.0 Study Timelines

9.1 Participants in the TT-C arm will be asked to complete the intervention within one month. They will also be asked to complete follow-up surveys up to 3-months post-baseline. Participants in the SOC arm will also be asked to complete study activities up to 3-months post-baseline. Of note, those in the SOC arm who decide to access the TT-C app after the 3-month follow-up survey will be asked to complete additional surveys at 4- and 6-months post-baseline.

Recruitment of subjects is expected to be completed within 9 months of study launch. Primary outcome analyses are expected to be completed with 6 months of end of data collection.

10.0 Inclusion and Exclusion Criteria

10.1 All potential participants (whether recruited online or in-person) will complete an online screening survey via Qualtrics and REDCap to obtain consent to be screened and verify all inclusion criteria. Screening may occur on the same day as enrollment or beforehand. The online screening survey will begin with a script that will be read by participants to explain the purpose of screening and clarify that if they are eligible, they will be invited to participate in the study. The script will also provide general information about the research study, the nature of the screening questions and related potential risks, the approximate length of the screening (~5 minutes), the confidentiality of the screening information, the use of any screening information obtained, the ability to skip any questions or withdraw at any time and contact information of key study personnel. After reading this screening script, participants will be asked if they are interested in participating and agree to voluntarily complete the screening procedure. Participants will electronically indicate their agreement and then take the survey.

Those who meet eligibility criteria will be asked to record the first name, e-mail, and phone number if interested in participating; those disinterested in participating can decline by exiting the website. Potential participants who do not meet eligibility criteria will be asked if they would like to be contacted about other research studies and, if so, to provide contact information.

10.2 Inclusion Criteria:

- Ages 18-29, inclusive

- Identify as African American/Black
- Able to speak and read English
- Has access to personal smartphone
- Current resident of AL, GA, NC

Exclusion Criteria:

- Aged younger than 18 years or older than 29 years
- Does not identify as African American/Black
- Non-English speaking
- Does not live in AL, GA, NC
- Unable to provide informed consent
- Receipt of full COVID vaccine series (including vaccination and booster or prior participation in a vaccine trial)

10.3 Special populations:

- This study will not include adults unable to consent
- This study will not include individuals who are not yet adults (infants, children, teenagers)
- This study *may* include pregnant people as they are not specifically excluded. Their status as pregnant should not affect their ability to complete any of the outlined study activities, nor should the outlined study activities affect their pregnancy
- This study will not include prisoners

11.0 Vulnerable Populations

11.1 NICHD has concluded that this protocol does NOT meet Federal requirements governing prisoner participation in human subject research and should NOT be considered by local IRBs for the recruitment of prisoners. Subjects enrolled who subsequently become incarcerated or are placed in detention may not continue study participation. Study visits cannot be conducted during the period of incarceration or detention

12.0 Local Number of Subjects

12.1 N/A

12.2 N/A

13.0 Recruitment Methods

13.1 Our recruitment strategy includes: 1) free and paid advertising and posting on social media sites; 2) advertising through targeted patient recruitment companies; 3) distribution through national organizations working with AA-YA, including HBCUs; and 4)

distribution through our community partners and other network collaborations.

13.2 Participants will be sourced from 1) social media sites; 2) targeted recruitment companies; 3) distribution through national organizations working with AA-YA, including HBCUs; and 4) our community partners and other network collaborations in AL, GA, NC.

13.3 We will use methods successfully deployed in our prior studies to recruit through social media sites frequented by AA-YA and rely on our strong network of community and academic partners for additional dissemination. Recruitment procedures may vary slightly depending on the community organization and study phase, which will be negotiated prior to the beginning of each phase of the study. For the focus groups and RCT, we will also follow respondent-driven sampling (RDS) methods and use a long-chain referral method to supplement recruitment.

13.4 We will use text and photos in combination for the Tough Talks - COVID research study recruitment campaign. One or more text elements will be combined with photos to create engaging advertisements. The language, photos and graphics might be used alone or with text statements on a variety of online platforms including but not limited to, websites, social media, online news outlets, mobile phone apps, social networking sites, micro-blogging outlets, photo sharing portals, etc. The language and images may also be used for printed materials, including but not limited to buttons, stickers, palm cards, flyers, and print advertisements. All ads will identify Tough Talks - COVID as a research study. A detailed recruitment plan providing example advertising text and images is appended to the IRB submission.

13.5 TT-C arm participants are compensated (using an e-gift card) for completion of baseline ($50), 1-month ($50), and 3-month surveys ($50), $50 for completing 75% of the app activities, and $50 for exit interviews (up to $250 in total). These participants will also be given the opportunity to complete an optional module of questions about Monkeypox as part of the baseline survey for an additional $10. In total, TT-C arm participants could be compensated up to $260.

SOC arm participants are compensated (using an e-gift card) for completion of baseline ($50), 1-month ($50), and 3-month surveys ($50) (up to $150 in total). These participants will also be given the opportunity to complete an optional module of questions about Monkeypox as part of the baseline survey for an additional $10. If an SOC arm participant decides to engage with the TT-C app when offered after the 3-month follow-up, they could complete an

additional survey at 4- and 6-months post-baseline, for $50 each, and $50 for exit interviews. These participants will also receive a $50 completion incentive if they complete at least 75% of the app activities. In total, SOC arm participants could be compensated up to $360.

13.6 *N/A*

14.0 Withdrawal of Subjects

14.1 The principal investigator has the authority to withdraw any participant at any time if in their opinion it would be in the best interest of the participant. The participant will be informed of this withdrawal and explained the rationale. Withdrawal will be documented in the study tracking system.

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

a. The subject withdraws consent/assent

b. The study is cancelled by the NIH (or other administrative entity)

c. The study is cancelled for other administrative reasons

d. Death of the subject

14.2 Participants may end their participation in the study at any time. No further data collection will occur from the date the decision is made to permanently discontinue the subject from the study. Participants who experience distress during the study while at the community partner organization will be offered counseling on site. Participants who experience distress during the study and do not come to the partner organization for a visit will be provided a list of community referrals via phone or e-mail. Any unexpected adverse events that meet the unanticipated problem (UP) reporting criteria will be immediately reported to the IRB of record and the respective sites' IRBs if applicable. A Study Stop Form will be completed at this time.

14.3 No further data collection will occur from the date the decision is made to permanently discontinue the subject from the study.

15.0 Risks to Subjects

15.1 We identified the following as possible risks to subjects and describe below how we plan to address those risks:

Breach of Confidentiality: A potential risk to participants is violation of confidentiality. We will take the utmost caution to protect the confidentiality of all responses. We will minimize this risk by maintaining confidentiality and discretion throughout all aims of the

study. Files – audio, paper and electronic– will not have any identifying information about the study participants and will be tracked through a unique SID and participant code. All audio recordings will be downloaded and stored on a password-protected, encrypted computer in locked offices at FSU and subsequently transferred to FSU encrypted servers. Transcription of audio files will be conducted using a HIPAA-compliant transcription service. Any names mentioned in the audio files will be redacted during transcription. Interview transcripts will be kept on FSU secure servers. Analysis of transcripts will be conducted on a password-protected, encrypted computer. Hard copies will be kept in locked files. We will take every available step to minimize the risk of identifying/linking data being subpoenaed, stolen, or inadvertently released. First, the Tough Talks-COVID study team has acquired a Certificate of Confidentiality from the NIH. Second, the study will safeguard against the risk of the linking information being stolen by keeping such information in a locked Excel spreadsheet on a secure server at FSU to which only essential study personnel who have completed CITI certification for human subjects research ethics training (http://citiprogram.org) will have access. We have also included numerous features to ensure app security and privacy. All relevant app communications (e.g. those between participants or those between participants and staff) will be secured via industry standard encrypted SSL communications links. These connections will ensure that all communications are inaccessible to unauthorized third parties. Furthermore, the app can be updated regularly to address any unforeseen security updates to the software libraries underlying the secured communication links. Beyond encrypting communication, users will need to log in with a username and password to access the app, even if the use of their phone is "unlocked." This will allow the user to share their phone generally with others without granting access to TT-C app. These software security solutions will provide the layers of both communications security and physical access security to ensure that only authorized users have access to the information stored on the phone as well as the information being shared over communications links. We will take special care to ensure that TT-C addresses participant privacy. During app onboarding, study staff will assist youth in choosing a discreet and anonymous username. Moreover, mobile phone screens themselves are also constructed to prevent surreptitious observation.

Emotional discomfort: It is possible that the study may precipitate discomfort and/or an emotional response when AA-YA answer questions about potentially sensitive topics such as medical mistrust. Further, participants may feel embarrassed about discussing sensitive issues. All participants will be told during the informed consent

process that their participation is voluntary and that they can chose to stop participating at any time without any consequences. Based on our experiences using similar data collection methods with youth in past studies, the likelihood and seriousness of this risk is minimal and we will strive to create a safe and comfortable environment for all study participants.

All sites have specific policies governing the treatment of human subjects. These policies specify that medical and psychological assistance will be available in the immediate environment in the event a participant should experience any adverse reactions resulting from study procedures.

While participants will be informed that they may refuse to answer any question at any time, responses or reactions to certain questions may indicate distress on the part of the participants. If at any time during the study, a participant divulges that he or she is at risk for harm, including but not limited to being abused or experiencing violence, if harm is suspected or likely, or if the participant states he or she is suicidal/homicidal, measures will be taken to ensure his or her safety. Reporting will be done as appropriate to the situation and the legal statutes, including reporting to child protection agencies or other appropriate agencies and referrals will be provided to appropriate support, counseling, or treatment resources.

15.2 *N/A*

15.3 *N/A*

15.4 *N/A*

15.5 *N/A*

15.6 *N/A*

16.0 Potential Benefits to Subjects

16.1 The risk to individual participants is small and the potential benefit to both the individual and society is substantial. The main benefit of the proposed study to society is the development of a potentially feasible and acceptable mobile app that promotes autonomy and improves COVID-19 vaccine uptake amongst AA YA and their social networks. This study is poised to reduce COVID morbidity and mortality among AA YA and their social networks, including peers and older adults. Therefore, the risk/benefit ratio is favorable.

16.2 Participation in this study may result in no direct benefit to participants.

17.0 Data Management and Confidentiality

17.1 Sample Size Considerations: Sample size calculations were conducted using simulation methods. The simulations: a) Step One: specify probabilities of vaccination and sample sizes for the three treatment groups and draw random samples of the specified sizes from binomial distributions with the specified probabilities treated as binomial parameters; b) Step Two: compare the outcome rates in the three samples using logistic regression and record whether the 2 degree-of-freedom test for differences is statistically significant; c) Step Three: make pairwise comparisons treatment arms using logistic regression; and d) Step Four: Repeat process 1,000 times and calculate power as the proportion of data sets (of 1000) generating statistically significant results.

Power calculations were conducted assuming that dropout would be equivalent across arms, and that approximately 15% would be loss to follow-up; therefore, assuming 250 306 participants will complete the primary endpoint assessment (125 153 per arm). Exhibit 1 depicts graphically the estimated detectable effect sizes (as a difference in proportion receiving any COVID vaccine) we will have 80% power to detect given a sample size of 250306, range of control arm rates of vaccine uptake, and assuming two-sided α=0.05. If the rate of COVID vaccination in the control arm is between 10-20%, we will have 80% power to detect a difference in vaccination of 1312-146% between arms. If the rate of vaccination in the control arm is higher (30%), we will have 80% power to detect a 1715.5% difference in vaccination rate between arms. The detectable effect size is lowest highest when the control proportion is closer to 50%, but we will still have 80% power to detect a difference of 17.616% if the rate of vaccination in the controls is 50%. We anticipate vaccination rate in the control arm will be low given that vaccines have been available for some time. Therefore, we expect a total sample size of 300 360 will provide sufficient power to detect a clinically meaningful difference in vaccine uptake.

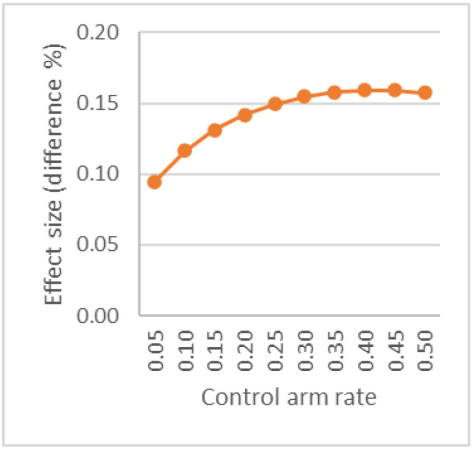


Exhibit 1. *Estimated detectable effect size with an effective sample size of 306 (153 per arm) and range of possible vaccination rates in the control arm; 80% power and two-sided alpha of 0.05.*

Effectiveness Outcomes: Primary effectiveness outcomes are COVID vaccine uptake and completion of series; secondary effectiveness outcomes are VH[20], confidence[53], and knowledge, attitudes, and beliefs.[54] We will also collect implementation outcomes, SCT constructs targeted by TT-C, COVID-specific risks and behaviors and pertinent constructs that have been validated in the extant literature on AA-YA (Table 5).

Analyses of Effectiveness Data: We will use logistic regression to determine the effect of treatment arm on the probability of vaccination uptake (yes/no) and COVID vaccine series completion (yes/no) at month three . We will determine whether the overall 2-degree-of-freedom test for differences among treatments is statistically significant. If so, we will examine the parameter estimates and standard errors to determine where difference lie between the three arms. We will focus on the odds ratios for comparing the probability of infection in each of the two treatment groups with the probability in the controls. The secondary outcomes of VH[20], vaccine confidence[53] and vaccine knowledge, attitudes and beliefs[54] will all be assessed using previously validated scale scores, each of which will consist of the continuous sum of responses to a series of questions with Likert scale responses. We will use linear regression models with treatment group as the exposure to determine whether secondary outcomes vary among treatment groups. Lastly, we use the causal mediation framework proposed by Valeri and Vanderweele to understand mechanisms for any intervention effects through each of our hypothesized mediators.[55-58] We will use the gformula command in Stata which uses the mediational g-formula to estimate the controlled direct, natural direct, and natural mediated (indirect) effects.[59]

Implementation Outcomes and Analysis: We will conduct qualitative interviews with a group of purposively selected AA-YA participants (est. n=12-16) and site staff (est. n=6-8) to assess barriers and facilitators to TT-C intervention implementation. We will conduct 12-16 in-depth exit interviews (~4-6 per state) on a rolling basis after participants have concluded the 3-month study cycle. All interviews will be audio-recorded and transcribed verbatim. Qualitative analyses will be conducted in the NVivo coding program. From AA-YA, we will ask questions on how sociocultural non-intervention contexts affected the likelihood of vaccine acceptance, vaccine series completion, and VH. From staff, we will collect qualitative data on

the inner and outer contexts affecting implementation with ongoing fidelity such as on policies, environment, funding, and social conditions that could influence intervention scale-up and sustainment. Due to the urgency of addressing COVID VH, we will use Rapid Content Analysis that is routinely leveraged in implementation science to assess and disseminate results quickly and accurately.[60] Findings will be explored as a function of participant age, sex, state, and setting. Qualitative findings will provide a direct line into real-world implementation considerations.

Note: Any deviations from the analysis plans outlined above or in the sections that follow will be documented and justified in the Statistical Analysis Plan developed for this protocol.

Qualitative Data Analysis: FSU will use NVivo software to perform all qualitative analyses. NVivo is a web-based application for organizing and analyzing textual, audio, and video data (qualitative) along with outstanding functionality for their integration with survey, test score, ratings, and demographic data (quantitative). NVivo employs the highest levels of data encryption available for a web application in all data storage, back up, and transmission. NVivo allows for project specific encryption feature.

Missing Data: In sensitivity analyses, we will also use inverse probability of treatment weights (IPTW) to account for missing data and potential differential retention between study arms over the study period. We will weight outcome models using stabilized inverse probability-of-censoring weights that include treatment arm as a predictor to account for differential loss to follow up. Pooled logistic regression models will be used to estimate the numerator and denominator of censoring weights, and weights will be multiplied over time.[15,16,61] The denominator will be calculated using a logistic regression model for loss to follow up, including treatment arm. Weights will be stabilized to reduce potential bias from extreme weights. Numerator weights for the stabilized IPTW will be estimated using a logistic regression model for loss to follow up without covariates. Distributions will be examined to ensure weights have a mean of 1; extreme weights that may introduce bias will be trimmed by cutting the top or bottom 1%. Analogous weight will be calculated for missing data, including relevant covariates, and will be multiplied by censoring weights.

Several procedures will be used to conduct data analysis when data for either outcomes or covariates are missing. The first step will be to assess the extent and pattern of missing data. If data are missing for only a few cases, then data analysis will be conducted only on study participants with complete data. However, when such a

strategy would result in loss of data from a substantial proportion of participants, or if this approach would lead to biased or inaccurate results, then some form of imputation will be performed. The form of imputation used will depend on the nature of the data that are missing. For example, data that are collected repeatedly might be imputed using the "last value carried forward" method; and in some instances, interpolation between neighboring points might also be used.

When the primary endpoint is missing, one data analysis will be conducted using only cases with the endpoint. Subsequent analysis will be done where missing endpoints are imputed. Hot-deck imputation or regression imputation may also be used in this context.

17.2 We will monitor recruitment and retention rates, site compliance with study procedures, and provide technical assistance for queries and concerns. Encrypted data will be saved on an FSU server, with password protection. We will examine data quality weekly (e.g., missing data, assessment of distributional assumptions, identification of outliers) and before statistical analysis is conducted. Comparability between participants across all three arms will be reviewed. Missing scale data will not be estimated. Comparability between sites and states will be examined. Data will be aggregated for general analysis purposes; however, if significant differences emerge, separate analyses comparing outcomes between sites or states detailing differences will be conducted.

Investigators receiving federal funding must adhere to the Code of Federal Regulations (CFR) to protect research participants and produce reliable study information. Sites participating in research sponsored by the NICHD need to have an internal quality assurance (QA) plan that will identify problems and correct errors in research study records.

Site monitors may visit participating study sites to review a selected portion of the individual participant records, including assent/consent forms, CRFs and supporting source documentation to ensure the protection of study subjects, compliance with the protocol, and accuracy and completeness of records. Regulatory files, as required, will also be inspected to ensure that regulatory requirements are being followed.

The site investigator will make study documents (e.g., consent forms, case report forms) and pertinent hospital or clinic records readily available for inspection by the local IRB, the site monitors, the NICHD, the Office of Human Research Protection (OHRP), or the sponsor's designee for confirmation of the study data.

17.3 We will take every available step to minimize the risk of identifying/linking data being subpoenaed, stolen, or inadvertently released. First, per Section 2012 of the 21st Century Cures Act as implemented in the 2017 NIH Certificates of Confidentiality Policy, all ongoing or new research funded by NIH as of December 13, 2016 that is collecting or using identifiable, sensitive information is automatically issued a CoC. As noted on the NIH website (http://grants.nih.gov/grants/policy/COC/faqs.htm#187), a Certificate of Confidentiality will help the research team "...avoid compelled 'involuntary disclosure' (e.g., subpoenas) of names and other identifying information about any individual who participates as a research participant (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect." We have applied for and received Certificates of Confidentiality for other NIH-funded research projects, and given the sensitive nature of the data collected for this project, do not foresee difficulty securing one for this study. Second, all research staff members are required to complete ethical clearance certification regarding protection of human's subjects through their relevant IRBs. Third, all studies will have documented procedures to safeguard against the risk of the linking information being stolen by keeping such information in locked spaces to which only essential study personnel who have completed CITI certification for human subjects research ethics training (http://citiprogram.org) will have access.

17.4 *N/A*

17.5 *N/A*

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

18.1 Site staff must first follow their own IRB's procedure for reporting and managing untoward effects.

There are three types of untoward effects to be identified: (1) those related to the participant, (2) those related to the study staff, and (3) those related to the neighborhood/community.

First, the study will catalogue any untoward effect related to the participant. Reporting is required for occurrences including social harms, psychological distress and serious life-threatening events such as suicide attempts. These may be immediately apparent to the study staff, such as the participant's emotional upset requiring referral for counseling; or they may be delayed and reported later to study staff, such as physical harm to an individual for having participated in the study. Study staff will notify the team of these untoward effects using a query system. Study staff will be briefed

during the training on the scope of possible untoward effects and instructed to report events.

Second, study staff may encounter untoward events during study visits that personally affect them. Training and guidance will seek to minimize this risk. Nonetheless, an assessment of the cost of conducting this study must include cataloguing these events as well. The protocol chairs should be notified of these events so that they may be immediately addressed, evaluated, and guidance modified or expanded to minimize similar risk to other staff.

Third, a critically important area any community-based study intends to evaluate is the impact, including untoward effects, of the project on the community. This will be done informally for this protocol with untoward events being reported to the protocol team.

All untoward effects/adverse events/unanticipated problems will also need to be reported to the FSU IRB if they meet all three of the following criteria:

"Unanticipated problems involving risks to subjects or others" (UPIRSO) refers to any incident, experience, or outcome that:

is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

is related or possibly related to a subject's participation in the research; and

Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Events that meet the criteria for an UPIRSO and are also serious adverse events should be reported to the FSU IRB within one (1) week of the investigator becoming aware of the event. Any other events that meet the criteria for a UPIRSO should be reported to the IRB within two (2) weeks of the investigator becoming aware of the problem.

If the report cannot be completed in its entirety within the required time period, a preliminary report should be submitted. The report should be amended once the event is resolved and/or more information becomes available

19.0 Provisions to Protect the Privacy Interests of Subjects

19.1 All questionnaires, evaluation forms, reports, and other records will be identified by a coded number and initials only, to maintain participant confidentiality. All records with personally-identifying information will be kept in a locked, limited access area (such as a locked file cabinet). All computer entry and networking programs will be done with coded numbers and initials only. Every effort will be made to ensure that study participants are protected from risks. The main risk breach of confidentiality.

19.2 Participants may be concerned about the security of their data, particularly since it is collected and stored electronically. Research staff at FSU have significant experience developing security protocols for Internet-based studies, and we will take a variety of steps to ensure participant security, including using a dedicated server behind a firewall, encryption of data, separation of identifiers from responses, and password-protected access to data.

For the Tough Talks intervention arm, participants will create a unique username that does not contain any identifying information but will be their username on the app. Participants will not be able to privately communicate with each other on the app. Trained research staff at Florida Stata University will monitor the website daily to ensure violations to privacy.

19.3 N/A

20.0 Compensation for Research-Related Injury

20.1 N/A

20.2 N/A

20.3 N/A

21.0 Economic Burden to Subjects

21.1 Participants should not incur any costs for their involvement in the activities described in this protocol.

22.0 Consent Process

22.1 Informed consent will be obtained from participants prior to completion of any study activities. Study staff will follow HRP-090 (SOP: Informed Consent Process for Research). The informed consent process will occur online prior to completing any study procedures. Eligible participants will receive the electronic consent delivered via email. Once they have electronically signed the consent form, they will be sent the online survey hosted by REDCap.

Non-English Speaking Subjects

- *N/A*

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- An online consent process for the eligibility screening is proposed. The introduction to the screening interview includes all the required elements for consent (45 CFR 46.116). No identifying information on volunteers is recorded during the online screening until a participant is determined eligible (i.e., by marking "I do consent to be screened for eligibility"). Therefore, there will be no identifying link of who agreed to be screened or not screened for the study. In addition, the screening presents minimal risk to participants and involves no procedures that would require written consent outside of a research context. Under these conditions the IRB is authorized to modify the requirements to obtain a signed consent form for some or all subjects (45 CFR 46.117 [c]).

Subjects who are not yet adults (infants, children, teenagers)

- *N/A*

Cognitively Impaired Adults

- *N/A*

Adults Unable to Consent

- *N/A*

23.0 Process to Document Consent in Writing

23.1 Study staff will follow HRP-091 (SOP: Written Documentation of Consent) by ensuring participants electronically sign the consent document (via REDCap eConsent).

23.2 *N/A*

23.3 The consent document to be completed by participants is appended to the IRB submission.

24.0 Setting

24.1 This is a fully remote (virtual) study. Qualitative interviews will be completed via a HIPAA-compliant teleconferencing software (e.g. Zoom).

25.0 Resources Available

25.1 The study team has significant experience with the conduct of internet-based recruitment and virtual/remote enrollment and completion of study activities. All staff will be adequately trained on the protocol and will practice assigned study activities before engaging with prospective or enrolled participants. Study team members will meet regularly (with the Lead PI present) to ensure proper implementation of study procedures, as outlined in the protocol. A study coordinator will be designated to coordinate all study staff, training, and activities.

26.0 Multi-Site Research

26.1 A total of 360 participants will be enrolled in the RCT phase of this study.

26.2 All sites will follow the recruitment procedures outlined above. There will be no modification of materials per site.

26.3 The following are responsibilities of the Reviewing IRB:

- Documenting IRB determination and provision to relying sites
- Provision of IRB-approved materials to lead study team
- Provision of consent form templates to relying site study teams
- Provision of relevant IRB policies to lead study team

The following are responsibilities of the Relying IRB:

- Conflict of interest management for relying site staff
- Study team training/qualification provision to reviewing IRB
- Provision of local context information to reviewing IRB
- Incorporation of site-specific consent language

The following are responsibilities of the Lead Study Team:

- Preparation and submission of study-wide application
- Preparation and submission of site-specific application(s)
- Provision of IRB-approved documents to relying sites study teams
- Provision of consent form templates to relying site study teams
- Collection and submission of information for continuing review
- Reporting of reportable events (unanticipated problems, noncompliance, subject complaints, etc.)
- Provision of information necessary for study closure

The following are responsibilities of the Relying Study Team:

- Conflict of interest management for relying site staff
- Incorporation of site-specific consent language

26.4 N/A