# Addressing COVID-19 Testing Disparities in Vulnerable Populations Using a Community JITAI (Just in Time Adaptive Intervention) Approach: RADx-Underserved Populations (RADxUP) Phase III

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| **Protocol Title:** | Influencing Factors of COVID-19 Testing: Main Study 2024 |
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| **Study Coordinator:** | Maribel Sifuentes, Manouchehr Hessabi, Anais Mendiola |
| **Population:** | 431 individuals in the intervention group, Male, Female, 18-89, general population sample drawn from the community through door-to-door outreach and community events in Northeast Texas, Harris County, and South Texas. |
| **Number of Sites:** | Three sites: Houston, Lower Rio Grande Valley, and Tyler, UT Houston is the lead site of the multi-site study |
| **Study Duration:** | The study will run from July 2024 - February 2025 |
| **Subject Duration:** | Intervention study participants will be enrolled, complete a baseline survey, and participate in a text message-based educational intervention throughout the study. They will be followed up by phone or in person for 8 weeks. For the control group participants' information, we will use a historical control group (the Control group from the phase II Embedded Study trial that completed a baseline and follow-up survey). |

**General Information**

RADx-UP is an ongoing research study funded by the National Institutes of Health to address COVID-19 testing disparities in vulnerable populations. The goal of RADx-UP is to reduce the burden of disease in vulnerable populations known to be at increased risk of severe COVID-19 infection (e.g., those with medical comorbidities, homeless, racial/ethnic minorities who live in rural communities). The focus of the Phase I main RADx-UP study was to examine COVID-19 testing to reduce infection transmission and prevalence. There are three sites (Houston, Northeast Texas, and South Texas). The Phase I main study questions were answered (approved under another IRB protocol) in a Randomized Control Trial (RCT) where 120 priority block groups were randomized to one of three conditions: 1) Multi-Level Intervention (MLI) group; 2) Community JITAI (Just-In-Time Adaptive Intervention) 3) Control group. The outcomes of this study were measured at the population level, and no individual data was gathered.

In Phase II, the embedded study was built off this main trial with some adjustments to the design because of expanded research priorities to include factors influencing antigen testing. The intervention priority census block groups (PBGs) that received either form of intervention in the main trial were combined into one pool of intervention PBGs for the embedded study. The control PBGs from the main trial remained the pool of control PBGs for the embedded study. A sample of intervention PBGs were randomly selected from across the three study regions and assigned to one of two intervention study arms. A sample of the control PBGs was randomly selected from across the three study regions and assigned to the control condition. We are recruiting and enrolling individuals from the selected PBGs across the three arms using systematic sampling with a random start.

In Phase III, we will build off of the Phase II embedded study with some adjustments to the design to address new research priorities that examine an intervention that is network informed and delivered through community health worker interactions plus digitally-delivered intervention content with the goal of increasing COVID-19 testing and vaccination. This model, if proven effective, can be scaled up to address COVID-19 and other future pandemics. We will utilize the sample of intervention PBGs used in Phase II and will recruit and enroll participants not previously enrolled in either phase I or II from these PBGs using convenience sampling methods. We will use a historical control group consisting of participants from our control arm in Phase II who completed both their baseline and follow-up surveys embedded in the study.

**Background Information**

Vulnerable populations in the U.S. experience significant COVID-19 disparities[1-4], and individuals with medical comorbidities have suffered disproportionately. Additionally, Hispanics are 1.5x more likely to be infected, 2.3x more likely to be hospitalized, and 1.8x more likely to die from COVID-19 compared to White, Non-Hispanics. Blacks are 2.4x more likely to be hospitalized, and 1.7x more likely to die.[5] The Phase III main study builds on our RADx-UP Phase I and Phase II work reaching these populations in three racially diverse regions: Houston/Harris County, South Texas, and Northeast Texas, leveraging the partnerships and resources of the Center for Clinical and Translational Science (CCTS) to increase SARS-CoV-2 testing, vaccination, and mitigation behaviors to reduce COVID-19 among underserved populations in Texas. The pandemic landscape and people's experiences with testing, infection, and vaccination have changed dramatically over the past two years. Vaccines have become available, testing access in local communities has waxed and waned, and attitudes toward COVID-19 severity and susceptibility have changed.[6]

Antigen self-testing kits are more available at this stage in the evolution of COVID-19, but among vulnerable populations, use is still low,[7] and instructions for antigen testing are not typically designed for low health literacy populations. Navigating the shifting testing-decision landscape is confusing to the public (test availability for free versus charged or requiring insurance; testing and vaccination locations change; PCR versus antigen testing; home tests versus clinically delivered; symptom-based testing, exposure-driven testing, serial testing, resources to trust or not trust, etc.). Studies are needed to explore access and use of antigen tests, including serial testing among vulnerable populations, and studies are needed to examine if low health literacy designed interventions improve COVID-19 testing decisions and completion behaviors.

The proposed study will focus on understanding factors associated with *rapid* SARS-CoV-2 testing, specifically.

**Study Partners**
This proposal leverages long-standing community partnerships and resources building specifically on the CCTS community engagement component and other community and organizational partnerships developed through several programs and projects across the three Texas regions. These Community Stakeholder Advisory Groups in each region ensure that bidirectional communication about COVID-19 and the study activities are responsive to community input and deemed culturally appropriate and impactful. Our partnerships, including those with local health departments and hospital systems, have enabled data sharing and analysis of surveillance data. New organizations, such as the UTHealth Institute for Implementation Science and the Texas Epidemic Public Health Institute (TEPHI), will provide additional resources to enhance the proposed study.

**Objectives**
The primary objective of this study is to:

1) Determine the effectiveness of the adapted MC-NET-JITAI (Multilevel Community network-informed Just-In-Time-Adaptive Intervention) versus a historical control group.

**Study Design:**

***RADx-UP Phases I & II.*** (The parent studies) We conducted a three-arm group randomized trial to assess the impact of multilevel interventions influencing motivation and access to testing: Arm 1) Community Engaged Just-In-Time Adaptive Intervention (Community JITAI) where we met regularly with community partners and exchanged community-specific information about COVID-19 (testing, infection rates, etc), Arm 2) Standard multilevel intervention (MLI), and a usual practice condition. We randomized 120 PBGs identified as communities with high levels of disparities across our three geographic regions to each condition using a covariate adaptive Randomization (Minimization) Schedule.
The primary outcome for the Phase I and II studies was community-level SARS-CoV-2 testing (primarily PCR testing). This measure was assessed bi-monthly throughout the study. We also conducted an embedded panel study to 1) compare the effectiveness of the CHW-Facilitated Self-Sampling Intervention (FSSI) vs. CHW Testing Navigation Intervention (TNI). In the ongoing study, we also collected social network data on a sub-sample of individuals to explore the influence of social networks on testing decision-making and behavior.

***RADx-UP Phase III***: Our Phase III study design focuses on **vulnerable communities** selected to intervention and control conditions and takes advantage of the fact that these communities were randomized to conditions using methods to ensure balanced arms. In Phase III, we will combine the two intervention conditions (TNI & FSSI), and will receive the MC-NET-JITAI. The study will include PBGs from each of the two intervention conditions in Phase II; they will be matched to the comparison PBGs on variables such as size, vaccination and testing rates, and the disparities index with the control group. The intervention will last 8 weeks; individuals will be recruited and asked to complete a survey (including RADx-UP common data elements).

In Phase III, we will utilize a historical control group consisting of 400 participants from the control arm who completed the baseline and follow-up surveys in the Phase II embedded study.

In Phases I and II, the PBGs were selected from the Harris/South Texas/NE Texas region at the ratio of 2:1:1, that is, 20 PBGs of MC-JITAI arm in Harris, 10 in South Texas, and 10 in NE Texas. Among the 40 PBGs in the control arm, all remain in the control group. During Phase II recruitment, we identified PBGs where recruitment was not feasible due to various factors (ex., dangerous areas, largely gated

neighborhoods, neighborhoods with HOAs that did not permit us entry into the neighborhood, etc.). Recruitment in Phase III will occur only in PBGs where it is feasible to return.

**Random Selection of Intervention Individuals within the PBGs:**
Participants who live in a PBG randomized to the intervention arm will be invited to participate in the trial for that arm. In each of the selected intervention PBGs, individuals will be selected via convenience sampling procedures described below under sample selection.

**Study Population:**
In the intervention study arm, we will enroll up to 431 individuals and 400 historical control group participants.

**Inclusion/exclusion criteria for intervention study arm.** In this study, the inclusion criteria for the enrolled intervention study arm individuals include being aged 18 years to 89 years and having a smartphone that accepts text messages. The exclusion criteria will include: (1) having been diagnosed with COVID-19 in the past 30 days based on a positive test (antigen or PCR) or a clinical diagnosis, (2) having tested for COVID-19 with PCR or antigen test within the past 30 days, (3) not being available in the recruitment area in the next 60 days, (4) having been an embedded study participant and (5) having been a snowball study participant.

**Selection of the study population.** Three large regions of Texas: 1) Houston/Harris County; 2) Cameron County in South Texas; and 3) seven counties, including the city of Tyler in Northeast Texas. The communities prioritized in this proposal include populations with medical comorbidities, and underserved Hispanics and African Americans in three racially diverse regions: South Texas, Houston/Harris County, and Northeast Texas.

**Primary and Secondary Outcome Measures:**
The pre-post surveys will assess the following behavioral measures:

1. Primary Testing Outcome: COVID-19 antigen testing using individual-level data.
2. Secondary Vaccination Outcome: COVID-19 vaccination uptake using individual-level data.
3. Secondary Outcomes: Mitigation measures if a positive test is obtained including mask wearing, isolating, and notifying close contacts.

**Study Survey:** Project personnel will use the survey platform REDCap (Research Electronic Data Capture) survey software to collect the study survey responses from the participants who consent. The survey instrumentation is designed to capture all relevant demographic characteristics, personal history regarding COVID-19 infection (self, others), testing and vaccination behavior, and psychosocial determinants for testing and vaccination behavior. This survey is composed of all RADx Common Data Elements (CDEs) required by our funder, survey measures taken or adapted from extant COVID-19 health promotion research for our RADx Phase I 2-1-1 survey.

**Summary of Embedded Study Survey Constructs**

| Measures / Constructs | Questions | Citation/Tool |
|---|---|---|
| Testing behavior | Testing for COVID-19, ever tested, last 30 days, positivity, access to testing | Funder required items, Novel items |
| COVID-19 history | COVID-19 sickness, hospitalization (self or others) | Funder required items, Novel items |
| Intention to test | Likelihood of testing (ever, 30 days), intention to test as needed | Funder required items, Novel items |
| Self-efficacy to test | Certainty of ability to be tested given situational contexts | Adapted self-efficacy measures following Maibach (1995)[11] |
| Pandemic safety behaviors | Wearing masks in private settings, wearing masks in public settings, washing/sanitizing hands, intentional social distancing (Never, some of the time, very often, all of the time) | Adapted for CEAL Program from Center for Economic and Social Research Understanding America Study Coronavirus Tracking Survey. https://www.phenxtoolkit.org/covid19/source |
| Vaccination | Vaccine uptake, type, doses | Funder required items |
| Trusted Sources of Information | Sources of information (doctor, media, health department, etc) | Funder required items |
| COVID-19 Perceived Susceptibility/Severity | How concerned are you about contracting COVID-19? How likely is it that you will get COVID-19? | Savoia E. et al, 2021[8] |

**Study Procedures**

**Sample Selection via Convenience Sampling- Houston/Harris County and Cameron County**

Study personnel from the Houston/Harris County & Cameron County areas will prepare for each PBG randomized to the study by mapping all streets in the selected PBG using Google Maps. Study personnel (CHWs) will approach each house as they recruit through the PBG, skipping those homes where current or past Phase II embedded study participants live. The CHWs will work in teams. One member of the team will work one side of the street and the other will work the other side of the street, both following the same sampling protocol. There may be occasions when it is appropriate that both team members work the same side of the street approaching the same houses together. Each attempt, successful or unsuccessful, will be recorded on a tracking sheet with items such as date and time attempted, address, identifying characteristics of households approached, whether individuals fit the inclusion and exclusion

study criteria, whether individuals consented to the study, reason for refusal or no answer, whether the survey was completed, whether Wi-Fi was available and barriers to visiting completion.

In addition, study personnel from the Houston/Harris County & Cameron County areas will identify community organizations where recruitment may be conducted, as informed by the social network data. In collaboration with selected organizations, study personnel will screen organization/event attendees by introducing themselves and the study, verifying eligibility, and scheduling an appointment at the individual's home where the remainder of the baseline visit may take place (unless the participant prefers to complete the entire baseline visit at that time). Staff will primarily recruit community members at these community events, but recruitment strategies may include posting recruitment fliers/posters at collaborating clinics, organizations, and businesses. Interested individuals will then call the contact listed on the poster to get more information about the study and learn how to participate. Study personnel can then screen the individual over the phone and if eligible, can schedule an appointment at the individual's home, where the remainder of the baseline visit will take place. Each community-based recruitment attempt, successful or unsuccessful, will be recorded on a tracking sheet with items such as date and time attempted, address of the collaborating organization, whether individuals fit the inclusion and exclusion study criteria, whether individuals consented to the study, reason for refusal, whether the survey was completed, whether Wi-Fi was available and barriers to visiting completion.

**Sample Selection via Convenience Sampling- Northeast Texas Region**

Study personnel from the Northeast Texas region will approach each PBG randomized to the study by mapping out all streets in the selected PBG using Google Maps. On each PBG map, they will identify community organizations where recruitment may be conducted with priority to those shown as salient in the social network analysis. In collaboration with selected organizations, study personnel will screen organization/event attendees by introducing themselves and the study, verifying eligibility, and scheduling an appointment at the individual's home where the remainder of the baseline visit may take place (unless the participant prefers to complete the entire baseline visit at that time). Staff will primarily recruit community members at these community events, but recruitment strategies may include posting recruitment fliers/posters at collaborating clinics, organizations, and businesses. Interested individuals will then call the contact listed on the poster to get more information about the study and learn how to participate. Study personnel can then screen the individual over the phone and if eligible, can schedule an appointment at the individual's home, where the remainder of the baseline visit will take place. Each community-based recruitment attempt, successful or unsuccessful, will be recorded on a tracking sheet as described in the previous paragraph.

**Consent**

CHWs will approach each house or organization/event identified using the sample selection procedure described above with scripted information describing the research study, eligibility criteria, the Phase III main study survey, a COVID-19 resource flier, and the incentive for participating. If the resident is interested, the eligibility of individuals in the household will be determined using a brief screening based on the inclusion criteria described above. Participation will be limited to one person per household. If more than one individual in the home is interested and is eligible to participate, the person with the nearest birth date to the date of enrollment will be enrolled. Upon confirming eligibility and which household member will be enrolled, CHW will review the informed consent form on paper copy or

electronically and acquire the individual's signature confirming consent. The individual will receive a paper copy of the consent or receive it electronically for their records.

**Recruitment**

The participant's consent will be documented in REDCap survey software that was developed with a field to capture the participant's consent in participating in the study and the date that informed consent was confirmed. Once the participant's consent is confirmed, study personnel will administer the baseline Phase III main study survey. The baseline survey includes part A, which is completed at the actual time of enrollment. Part B of the survey will also be sent to the participant electronically so that they can complete those items at their convenience. The study staff will record the responses to part A of the survey for the participants into the REDCap platform on a The University of Texas Health Science Center at Houston (UTHealth) secured device. After part A of the survey is completed, study personnel will provide participants with a COVID-19 resource flier. If the participant does not have time to complete the baseline survey part A at the initial home visit, study personnel will make an appointment to either return within 7 days or offer to complete the survey option virtually. The entire visit (introduction, screening, and survey) may take up to 1 hour.

Upon completion of the baseline survey part A, the participant will receive the first incentive card valued at $50. Study personnel will also make an appointment for the 8 weeks follow-up post-survey to be conducted by phone (or in person, depending on participant preference) and obtain contact information to follow up throughout the 8 weeks period with intervention related messages or answer participant questions. The staff will send a reminder of the 8 weeks follow-up appointment to the participant. The time frame for the follow-up appointment will be determined by study personnel counting out 8 weeks from the initial home visit. However, because the participant's schedule and availability will be accounted for, the earliest this follow-up appointment can be completed will be 5 weeks from the initial visit and as late as the last day of data collection for that PBG, which could be approximately 4 months from the initial visit. The week and day prior to the post-survey appointment, study personnel will send reminders. The phone-based post-survey will take up to 30 minutes, and the participant will be issued a second incentive card valued at $35 for their participation in the post survey, which will be mailed or emailed to the participant by study personnel if the follow-up was done via phone. If the participant prefers, the follow-up appointment can be completed in person instead of over the phone, and the incentive will be given in person as well.

**Social Network Intervention**

***Social Network Data from Phase I & II.*** Our Phase I investigation of organizational networks identified and recruited organizations providing COVID-19 services and healthcare to compose inter-organizational networks in each study region. In Phase II, we recruited individual residents' door-to-door or from community organizations in PBGs to participate in our Phase II embedded study related to self-testing and their place affiliation history. As part of the data collection, which collects data on knowledge, attitudes, and testing behaviors, individuals completed an individual-level social network survey. These participants served as the seeds for a snowball sampling recruitment approach to identify the social ties among friends, family, and coworkers, composing communication networks through which individuals' access COVID-19 related support. Further, these social network survey respondents indicated affiliations with organizations as clients or members.

We linked Phase II personal network data with the organizational network data collected during Phase I to compose multilevel network structures for each region. In addition, in Phase II, these network survey respondents nominated individuals comprising their social networks and provided their contact information. The individuals comprising the seeds' social networks were then contacted to complete the same survey (1st snowball layer), who in turn nominated persons in their own social network. Individuals nominated by the 1st layer snowball participants were then contacted to complete the same survey (2nd snowball layer), but were not asked to identify their own social network. Nominated individuals were contacted by NetCollect software through email/messenger to complete a survey. Note that each household is a single node in the network, and while each seed can nominate and provide contact information for any individual in any number of households, they are limited to nominating one person per household.

***Social Network-Informed Intervention.*** We used the data gathered in Phases I and II regarding the social networks by region to identify nodes (individuals and organizations) with the greatest influence operationalized as specific network positions they occupy in Phase I and Phase II social networks in each region. We will approach the organizations that demonstrated influence to either let their constituents know about the study or allow us to partner with them and recruit from their location. We posit this strategy will enhance the impact of the reach and impact of intervention strategies.

**Project Materials**

**Intervention Arms:**

**Multilevel Community Just-In-Time Network informed Adaptive Intervention (MC-NET-JITAI):** As previously described, recruitment of participants to the MC-NET-JITAI will take place at the participant's home or at one of the salient community organizations that our participants look to and interact with around COVID-19 topics identified through the social network data. CHWs will consent and enroll participants in the MC-NET-JITAI from the randomized PBGs. MC-NET-JITAI will include Community Health Workers (CHW) providing the participant with a batch of 4 rapid antigen tests that can be shared with people in the household or other close contacts if needed, a COVID-19 resource flier tailored to the study region and updated information about COVID-19 testing and vaccination. The intervention will consist of enhanced behavioral and educational text messages, up to three messages each week, providing updates on COVID-19 testing and vaccination. The text messages will include digitally-delivered intervention content such as a video with low-literacy instructions for administering the rapid antigen tests, guidance if they tested positive (e.g., quarantine, notify contacts, wearing a mask), and other relevant strategies and content focused on increasing COVID-19 testing and vaccination. The CHWs will also be available by phone to the participants for any follow-up questions. CHW will follow up via text, email and/or phone with the participants during the two months post-enrollment. In addition to the intervention, the participants will be asked to complete the pre and post-test surveys. Post surveys will be administered online, over the phone, or in person two months after the initial intervention.

**Control Arm:**

**Control PBGs:** Since we are utilizing a historical control study design, we are not recruiting any new control participants for this Phase III main study. Instead, we will analyze the survey data already collected from the Phase II embedded study control participants.

**Ethics**

Participants will be approached at their home or at a community organization/event for enrollment. The trained community health workers will explain the study generally and ask if the participant would like to

hear more about the study. If so, the community health worker will review the consent document and answer any questions. The participant will decide whether or not to participate and sign the documents indicating consent. A copy of the consent will be provided to the participant. The consent forms will be stored separately from the data to protect the privacy of the subjects. A unique identifier will be created to link the baseline and follow-up surveys.

The protocol for this study will also be reviewed by UTHealth - Tyler as several investigators are from this institution and one of the three study sites is in the North East Texas / Tyler region.

**Data Management and Security**

**REDCap (Research Electronic Data Capture)**

REDCap is a secure web application for building and managing online surveys and databases. REDCap was developed by experts at Vanderbilt University with partial funding from NIH.
REDCap was designed to allow researchers with a robust data management plan to quickly define project-specific data capture forms and launch protocol in an accelerated period of time. [9] Research projects are inherently diverse and are developed independently by investigative teams across the spectrum of biomedical sciences. As such, these projects tend to have diverse data dictionaries to represent common data elements such as demographics, clinical findings, and laboratory results. Providing pre-built, shared forms may shorten the database development process while promoting harmonization of data collection. Although data collection form creation is straightforward in REDCap, researchers relayed early in the program their desire to reuse validated instruments developed previously by their own teams or by other research teams in the consortium. In addition to saving setup time for research studies, creating easily consumable, pre-defined data collection instruments from a shared library would facilitate the harmonization of data collection across multiple studies since they would be using a common data dictionary. [9-10]

We used these REDCap features to collect data from CHWs, tracking Phase III recruitment and collecting survey responses from enrolled participants.

REDCap data capture system is fully compliant with the FDA regulatory requirements. REDCap can be installed in a variety of environments for compliance with such standards as HIPAA, 21 CFR Part 11, FISMA (low, moderate, high), and international standards. REDCap is fully personalized to meet your security policies and user needs. The REDCap uses PHP + JavaScript programming languages and a MySQL database engine for data storage and manipulation. The system runs in Windows/IIS and Linux/Apache web server environments.[9] The diverse applications of REDCap include support of basic science research studies, data collection for clinical trials, registries and cohort studies, quality reviews for clinical practice, comparative effectiveness trials, patient questionnaires, clinical decision support applications, and operational support. [10]REDCap provides automated export procedures for seamless data downloads to Excel and common statistical packages (SPSS, SAS, Stata, R), as well as a built-in project calendar, a scheduling module, ad hoc reporting tools, and advanced features, such as branching logic, file uploading, and calculated fields. [9]

**Data Collection**

The front-end web app will be accessible to external users on the UTHealth School of Public Health web domain at https://redcap.uth.tmc.edu/. Project staff will be provided login credentials specific to their role. For instance, the research coordinator for the survey will have full administrative control over the local application and datasets stored in the back-end server, including the ability to create new projects, modify project components, adjust the survey programming, and export survey results in various formats at any time. "Lead" users will be able to initiate surveys, open and close surveys for editing, and send reminders to participants automatically via phone or email. "Leads" will also be able to track the progress of other projects, and staff during "Interviewers" will be able to navigate the application to administer surveys and to track recruitment following the procedures described above.

The project coordinator responsible for REDCap will perform quality assurance and quality control checks on the database collected weekly to identify inconsistent data points, missing data, and incomplete data collection.

Two forms will be prepared for each region. One form will be to administer and collect the Phase III main study survey among enrolled intervention participants and will be initiated by project staff in person upon enrollment. We will also use REDCap to administer follow-up surveys two months after the participant completes their first survey, which will be done during a phone call or in person with a staff member who records the responses. After multiple attempts to complete the survey via phone or in person, we will reach out to the study participant with a secondary option to complete the follow-up survey via email or text message.

All surveys initiated in REDCap will have a unique survey identifier for the individual participant and the region where the survey is taking place and will be automatically anonymized. Phase III main study survey responses will also be iterated with proper data points identifying the census block group where the participant was recruited.

All recruitment data and survey data collected for the Phase III main study will be recorded and maintained within REDCap at UTHealth per funder requirements. This dataset will include the funder required RADx Common Data Elements (CDEs) and additional measures assessing the primary outcomes of testing behaviors and their psychosocial and socioeconomic determinants. Additional quality assurance and quality control procedures will be completed on the CDEs per funder requirements and then uploaded on a regular schedule to the RADx-UP Coordination and Data Collection Center (CDCC). The data will be shared with the Duke Clinical Research Institute ("DCRI") in North Carolina. Duke was chosen by the NIH to hold the data from all RADx-UP studies. Duke will keep these non-identifiable data in a secure database for COVID-19 research at the NIH.

We are handling the data management and monitoring according to Good Clinical Practice Guidelines. This will ensure we meet the ethical and scientific quality standards for conducting trials (GCP) guidelines.[11-13] The principles of GCP help to ensure the quality and consistency of trial/study operations and data and may result in increased costs.[14]

**Data Monitoring and Data Management**

The quality of a clinical study is ultimately dependent on the integrity of the data collected during the study. Well-organized and reliable data are critical to the success of a study. Data management procedures are performed to maintain data integrity and to ensure the data generated during the study will arrive at the same conclusions and interpretations equivalent to those derived from clean data. This process includes 1) Data Monitoring, 2) Data Cleaning, 3) Missing data, and 4) Quality Control checks.

1) **Data Monitoring:** The RDCC has the overall responsibility for the trial's data monitoring. The RDCC personnel regularly conduct data monitoring to identify potential discrepancies in the data and communicate with the clinic to resolve the discrepancies. The primary focus for data monitoring is critical to protect human subjects, maintaining the integrity of study data, and compliance with applicable regulations. We will be devoted to assessing the critical study data and processes and evaluating significant risks and potential site non-compliance identified. Identify data entry errors (e.g., discrepancies between source records and case report forms (CRFs) and missing data in source records or CRFs; Verify that the study documentation exists (e.g., consent process is documented, etc.). Monitor the quality of the overall conduct of the trial at the study site (e.g., attention to detail, thoroughness of study documentation, appropriate delegation of study tasks, and appropriate investigator supervision of clinic staff performing critical study functions). In addition, we assess compliance with the protocol and investigational product accountability. A data monitoring report will be sent to the research coordinator and the PI. The monitor should follow up with the clinical site to ensure that the issues raised by the monitor are addressed in a satisfactory manner. The recommendations provided by the monitor are meant to ensure compliance and data quality and improve site practices that could result in inadequate human subject protection and/or poor data quality.
2) **Data Cleaning:** The RDCC Data Management group will conduct data cleaning for the trial. Data cleaning refers to a group of activities used to assure the completeness, validity, and accuracy of data. Data cleaning activities are including a) developing and running various rules to identify potential anomalies in the data submitted by the sites, b) creating an Edit Check Program (ECP) is created in SAS that check for missing data, implausible data (that which complies with the codebook but is not in the range/suspect), improbable data (potential outliers' lab values (Mean±5SD)), or for other measurements with normal distributions (Mean ±3SD). For skewed distributions this could vary between 4 SDs and 5 SDs, impossible data (does not comply with the codebook /incorrect), and c) protocol deviations. The participant information on paper CRFs and data entry into database will be done by research assistant/coordinator once the participant was enrolled in to the study and the initial study data collection is complete. Once the data are in the database, the Data Management Analyst at RDCC runs the ECP periodically, which checks that all required data in CRFs are entered into the database. The ECP will also look for missing and discrepant data. The list of missing and discrepant data will be communicated to research coordinator and the PI and sent for further checking/correction; any corrected data will again be entered into the database. Data cleaning will be done periodically (biweekly/monthly) until the errors are amended as an iterative process. The database is equipped to have audit trail. In this trial, we will also use Census data at the Block Group level to obtain certain information that is not available at individual level. This necessitates careful attention when merging data at individual and Block Group levels. The Census data at Block Group level is de-identified. Dr. Rahbar has worked on grants focused on assessing Social Disparities in Health using Measurement of Neighborhood Socioeconomic Characteristics.

3) **Missing data**: The enrolled individuals completing the follow-up survey constitute the analysis set. Every effort will be made to keep all participants in the study and to obtain required data at each scheduled time point. All information for patients who dropped out from the study will be recorded and stored in the database. Traditional regression techniques usually assume that all data are complete and will produce unbiased estimates and valid inferences under missing completely at random (MCAR) assumption. We will examine drop-outs, missing data and measurement errors which are common problems with longitudinal data structure to be able to identify accurate missing data mechanisms and patterns so that we can explain missing data mechanism. If the missing data are non-ignorable/informative in the sense that missingness may depend on the missing observations, modeling of the informative missing data or dropout processes will be conducted. An attempt will be made to incorporate the missing values mechanism into the model as discussed in Little and Rubin. All Analyses will be performed primarily using widely available tools in SAS® version 9.4 (SAS Institute, Cary, NC)[15] or R,[16] at a significance level of0.05.

4) **Quality Assurance (QA) & Quality Control (QC) Procedure** Upon completion of resolving data cleaning, the data quality control process will be initiated. The QC process involves 1) randomly selected patients (10-20%), 2) comparing source documents to CRFs, and 3) comparing CRFs with the database. In all processes, we will select critical variables that determine the safety/effectiveness of what will be used in statistical analysis.

**Data Safety and Monitoring Board (DSMB)** If needed, a Data Safety and Monitoring Board will be established to oversee the conduct of this study to ensure participant safety and quality of the data. The DSMB will be convened to monitor activities conducted at all intervention and control sites, and to oversee data collection and implementation at all community and clinic organizations. The functions of the DSMB include the following: 1) To review and approve a plan for data quality assurance and safety monitoring for this trial, 2) To review data on a timely basis, to ensure proper conduct and progress of the study, 3) To review credentials of all project staff and consultants with relation to data quality and safety, 4) To make recommendations to project investigators and staff regarding issues of concern, 5) To review and address any potential ethical issues, 6) To approve any changes made in response to recommendations made by the DSMB, and 7) To alert NIH to any concerns that are not properly addressed by the study investigators.

**Statistics**

**Statistical Analysis - Main Study Primary Outcomes**. We will conduct a series of analyses regarding the primary outcome variable - testing for COVID-19. First, we will conduct McNemar's test on data from the prospective cohort only. In addition to the test p-value, the odds ratio of COVID-19 testing for post-intervention versus baseline will be evaluated to assess the intervention effect. Second, based on both the prospective cohort and historical controls, we will find inferences for the ratio of odds ratios for intervention versus control. Third, using the prospective cohort, we will build a multi-level generalized linear mixed model (GLMM) including time as a fixed effect factor to evaluate intervention effect. Multiple random effects will be specified to account for the hierarchical structure of persons nested within PBGs nested within regions. Additionally, we will test variables such as individual demographics and baseline measures of rapid testing uses and include significant variables as the fixed effect factors. We will also test the PBG-level of Social Determinants of Health (SDOH) (e.g., % of minority, % of people with no insurance) to investigate the SDOHs as a potential effect modifier on the intervention effectiveness. We will also compute various network measures based on personal networks and organization affiliation patterns associated with COVID-19-related outcomes. Finally, we will build a GLMM to data of both the prospective cohort and historical controls. We will specify proper random effects to account for hierarchical nesting structure.

**Sample Size for Testing the primary hypothesis in this study**.
We have estimated the sample size of the prospective cohort based on the primary hypothesis that individuals experiencing the intervention of Phase III will have higher levels of effective use of SARS-CoV-2 testing than their testing at baseline. The McNemar test, together with the odds ratio (OR) of COVID-19 testing for post-intervention versus baseline, will be used to assess the intervention effect. Preliminary data yielded a discordance of 19% between baseline and follow-up measurements. The ORs were 3.4, 2.3, and 2.3 for Harris, Cameron, and NETX, respectively. The OR for the pooled data was 2.55. We use an OR of 2.5 and a discordance of 19%, which represents an 8% difference in the proportion of testing at follow-up compared to baseline, to size the prospective cohort. For a one-sided test at the significance level of 2.5%, a **sample size of 237 is needed to provide 80% power** for confirming the intervention effect. To allow for a **45% loss to follow-up**, **431** participants need to be enrolled at baseline. The table below provides the size options for a one-sided McNemar test of alpha 2.5% and power 80%.

| Proportion of discordance | Odds ratio (OR) | Difference in proportion of testing pertaining to OR | Required sample size | Enrollment allows for a **35%** loss to follow-up | Enrollment allows for a **45%** loss to follow-up |
|---|---|---|---|---|---|
| 0.19 | 2 | 6% | 393 | 605 | 715 |
| **0.19** | **2.5** | **8%** | **237** | **365** | **431** |
| 0.19 | 3 | 9.5% | 177 | 273 | 322 |
| 0.3 | 1.5 | 6% | 681 | 1048 | 1239 |
| 0.3 | 1.727 | 8% | 387 | 596 | 704 |
| 0.3 | 2 | 10% | 249 | 384 | 453 |
| 0.3 | 2.75 | 14% | 128 | 197 | 233 |

**Statistical Analysis - MC-NET-JITAI.** We will analyze the secondary outcome measures using the McNemar test, conditional logistic regression model, generalized linear mixed model (GLMM). The enrolled individuals completing the follow-up survey constitute the analysis set. In GLMM, we will specify proper random effects to account for hierarchical nesting structure. Secondary analyses will examine the relation between knowledge, attitudes, and intentions on testing and vaccination decisions and we will use the same multilevel GLMM models.

**Resource Sharing**. All unique research resources developed as part of the proposed collaboration between UTHealth, the University of Texas Health Science Center at Tyler (UTHSC-T), and other project partners will be made available to the public upon request at the end of the grant period. Examples include dissemination models, recruitment, and data collection protocols, as well as study instruments. All requests for research resources should be sent electronically to the primary PI.

**Data Sharing.** We recognize that the funder requires the RADx-UP testing intervention projects to use rapid scale-up of rigorous research strategies and integrate data collected across the sites to maximize improvements in public health control of the pandemic. Thus, to the extent possible, data acquisition, collection, and curation strategies will be coordinated with the CDCC guidance for annotation and benchmarking of data, including obtaining appropriate consent for data sharing. A data-sharing plan will apply to qualitative, quantitative, and process data collected during the research studies. Project study staff will make RADx-UP intervention data available after the primary finding's manuscript is accepted for publication or 18 months after Phase III study completion, whichever occurs first. The guidelines for data sharing and the use of multisite data in our region will be used for sharing data by the participating site in our proposal. The complete study data files, with sufficient data documentation for proper analysis, will be made available to the public on a secure website requiring password identification for access. The

final datasets will be stripped of all personal identifiers prior to release for sharing, but to ensure confidentiality of all participants, and that the data are used only for research, we will also require a data sharing agreement that provides for: (1) a commitment to using the data only for research purposes and not to identify any individual participant; (2) a commitment to using best statistical and ethical practices in analyzing and reporting finding; (3) a commitment to securing the data using appropriate information technology; (4) a commitment to crediting the source and the funding agencies of the original project in all publications and presentations; and (5) a commitment to destroying or returning the data after analyses are completed.

**Publication Plan:** The following guidelines have been established by our project, through a publication committee, for requesting data and for the utilization of data.

General Guidelines:
1) Data requested must be for the purpose of performing research and publishing the results. Any extrinsic use of this multisite data must be approved by our publication committee, including abstracts, manuscripts, public presentations, and preliminary data in grant applications.

2) The Publication Committee will review all proposals to ensure absence of conflict with previously approved proposals, determine merit, and record the date and the approval of proposals. Members of the publication committee will also have the opportunity to voluntarily assist with the proposed research and form a writing group.

3) The electronic dataset files will be stored in a confidential manner on a password-protected computer in a locked office or in a locked file cabinet in a locked office so as to protect the confidentiality of subject information, if applicable. Multisite data will not be released to individual PIs without written consent of all other site PIs who contributed data to the multisite data.

4) Errors and uncertainty are inherent in all data and any errors may affect the final results and research findings. For this reason, any data discrepancies or anomalies identified during data management and analysis can address these issues, maintain the quality of all data.

**ATTACHMENTS**

1. Consent document for the main study (English)
2. Consent document for the main study (Spanish)
3. Survey of enrolled participants in the Main Study (Bilingual- English and Spanish)
4. Recruitment poster (English)
5. Recruitment poster (Spanish)

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