

Community-engaged Optimization of COVID-19 Rapid Evaluation And Testing Experiences (CO-CREATE-Ex)

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Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
5.1 & 10.1.7	Study population updated to exclude children under 2 years old Data records retention updated from 2 years to 3 years	Children under 2 are not authorized to use the FDA-approved rapid antigen test kits NIH regulations require data to be stored up to 3 years after Final Expenditure Report submission.

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1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Community-engaged Optimization of COVID-19 Rapid Evaluation And Testing Experiences (CO-CREATE-Ex)
Study Description:	<p>Our goal is to use a flexible and sustainable approach that promotes responsiveness to both the needs of the community and the changing pandemic context while reducing COVID-19 testing disparities. This project will refine, and test three implementation strategies prioritized by our Community and Scientific Advisory Board (CSAB). These three strategies include:</p> <ul style="list-style-type: none">(1) current, walk-up free testing,(2) promotores-led COVID-19 test counseling and preventive care reminders,(3) vending machines that dispense FDA-authorized self-testing kits.
Objectives:	<p>Primary Objective: Our primary objective is to refine and operationalize our multi-component implementation strategy bundle and a related set of measures of success for rapid FDA-authorized COVID-19 rapid testing.</p> <p>Secondary Objectives: Our secondary objective is to implement and evaluate the impact of our innovative, multilevel, and multicomponent implementation strategy bundle to optimize COVID-19 rapid testing among underserved, Latino communities using a roll-out implementation optimization study design across four clinics over 18 months.</p>
Endpoints:	<p>Primary Endpoint: Using our partnership with the Global ARC and Community and Scientific Advisory Board, we will finalize and operationalize the implementation strategy bundle and measures of implementation and sustainment success within the first quarter.</p> <p>CSAB members will be provided with \$100 per meeting and a total of 10 CSAB meetings will be held across the 2 years of the project. Each session will be recorded and structured forms will be completed to document how our team engages with the CSAB members.</p> <p>Partner engagement surveys will be administered and analyzed after each meeting.</p> <p>Secondary Endpoints: We will roll out 3 strategies to optimize COVID-19 testing: 1. current, walk-up free testing.</p> <p>2. promotores-led COVID-19 test counseling, and preventive care reminders.</p> <p>3. vending machines that dispense FDA-authorized self-testing kits.</p> <p>For each strategy, participants will consent into the study, provide demographics and test history, and receive a free rapid antigen test (RAT) kit. See section 2.3.3 for more details</p>
Study Population:	<p>For the CSAB (Aim 1), a total of up to 18 members will be included. The CSAB will include: up to 6 community members (who may also be SYH patients) from the four areas from which we will conduct patient recruitment (San Ysidro, Chula Vista, Lincoln Park, Logan Heights), up to 6 clinical providers or administrators from SYH, up to 3 public health</p>

research partners, up to 2 policy partners, and 1 County of San Diego Health and Human Services partner. This CSAB will focus on the refinement and evaluation of the COVID-19 testing strategies. These individuals will comprise Cohort 1.

For Aim 2, individuals of all ages will be included in this study. Study enrollment will occur at San Ysidro Health (SYH) Clinics. Aim 2 will have 2 cohorts:

Cohort 2: Community members, SYH patients and non-patients (n= 7,500)

Cohort 3: SYH providers and staff (n= 12)

Phase:

Not applicable

Description of

4 clinical sites with San Ysidro Health Centers located in San Ysidro, Chula Vista, Lincoln Park, Logan Heights

Sites/Facilities Enrolling

Participants:

Description of Study

Implementation strategies include Walk-up on-site testing, Promotore-led testing navigation and general preventive care reminders, No-cost self-testing kit vending machines.

Intervention:

Study Duration:

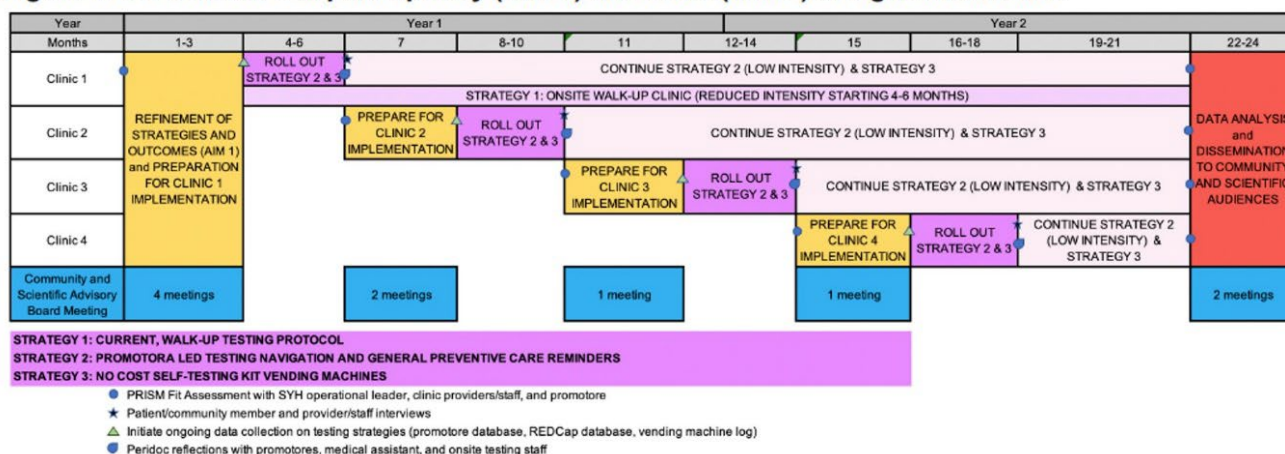
2 years

Participant Duration:

21 months

1.2 SCHEMA

Figure 1: CO-CREATE-Ex participatory (Aim 1) and ROIO (Aim 2) design and timeline



1.3 SCHEDULE OF ACTIVITIES (SOA)

Project Timeline										
Year	Year 1						Year 2			
Months	1-3	4-6	7	8-10	11	12-14	15	16-18	19-21	22-24
Finalize multicomponent strategy bundle and measures (Aim 1)										

Prepare for rollout of promotore model and vending machines including PRISM Fit Assessment for Clinic 1										
Clinic 1										
Roll out multicomponent bundle (adding promotores and vending machines)										
Reach, adoption, implementation, effectiveness data collection										
Clinic 2										
Review of data and refinement of program plans including PRISM Fit Assessment										
Rollout of multicomponent bundle										
Reach, adoption, implementation, effectiveness data collection										
Clinic 3										
Review of data and refinement of program plans including PRISM Fit Assessment										
Roll out of multi-component bundle										
Reach, adoption, implementation, effectiveness data collection										
Clinic 4										
Review of data and refinement of program plans including PRISM Fit Assessment										
Rollout of multicomponent bundle										
Reach, adoption, implementation, effectiveness data collection										
Sustainment period										
Continued delivery of promotore services and vending machines; low intensity walk-up services										
PRISM Fit Assessment for all Clinics										

Community and Scientific Advisory Board (CSAB)									
CSAB meetings	4 meetings (Aim 1)		2 meetings (Aim 2)		1 meeting (Aim 2)		1 meeting (Aim 2)		2 meetings (Aim 2)
Data analysis and dissemination									
Data analysis for the overall study about effectiveness and implementation outcomes over time									
Dissemination of results to community and scientific audiences									
Transmission of RADx-UP common data elements (CDEs) to the CDCC	Monthly throughout data collection								
Transmission of other project data to the RADx-UP CDCC	Quarterly throughout data collection								

Note: This is the planned timeline for the project and is subject to change based on logistical considerations (e.g., due to supply chain disruptions, we cannot be certain when the vending machines will arrive) and feedback from the Community and Scientific Advisory Board and the Community Health Partner.

2 INTRODUCTION

2.1 STUDY RATIONALE

There continues to be a need for COVID-19 testing that is pragmatic, community-centered, and sustainable. This project will refine, and test three implementation strategies prioritized by our Community and Scientific Advisory Board (CSAB). These three strategies include:

- (1) current, walk-up free testing,
- (2) promotores-led COVID-19 test counseling and preventive care reminders,
- (3) vending machines that dispense FDA-authorized self-testing kits.

Our goal is to use a flexible and sustainable approach that promotes responsiveness to both the needs of the community and the changing pandemic context while reducing COVID-19 testing disparities.

2.2 BACKGROUND

Throughout the COVID-19 pandemic, rates of COVID-19 have been persistently high in San Diego County's central and southern communities near the US/Mexico border. These regions predominantly house Latino residents, the ethnic minority community most impacted by COVID-19 in San Diego. In our Phase I RADx-UP project, UC San Diego partnered with San Ysidro Health and the Global Action Research Center, to co-create and demonstrate the impact of a PCR-based COVID-19 testing program in San Ysidro, one of the most impacted areas from COVID-19 in San Diego County. To date, we have tested

>10,000 community members (92% Latino) and received requests to scale-out the testing program to additional primary care clinic sites.

In this Phase III project, we will extend work with our Phase I community and clinical partners to refine, specify, implement, and evaluate an implementation strategy bundle that optimizes COVID-19 testing, expanding beyond current PCR testing to FDA-authorized COVID-19 rapid antigen testing.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Participants enrolled will receive an at-home antigen test kit to perform on themselves. Therefore, the risk for participating in the study is minimal as collection of the nasal swab is non-invasive and produces minimal discomfort. General discomfort may occur as participants are asked to discuss sensitive information during interviews and surveys.

2.3.2 KNOWN POTENTIAL BENEFITS

Participants will benefit from knowing their COVID-19 infection status in real time and will be able to adjust their behaviors to reduce exposure of their close contacts and family members. Additional benefits are increased participant engagement in their healthcare and comfort with use of technology to access healthcare. Overall proof of concept for use of technology for increasing healthcare access in underserved populations.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

The potential risks to participants are reasonable in relation to these anticipated benefits for the participants and others because all risks are assessed as being minimal and much can be done by the research team to protect against these risks.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
Our primary objective is to refine and operationalize our multi-component implementation strategy bundle and a related set of measures of success for rapid FDA-authorized COVID-19 rapid testing.	Using our partnership with the Global ARC and Community and Scientific Advisory Board, we will finalize and operationalize the implementation strategy bundle and measures of implementation and sustainment success within the first quarter. CSAB members will be provided with \$100 per meeting and a total of 10 CSAB meetings will be held across the 2 years of the project. Each session will be recorded and structured forms will be	These endpoints have been previously used in our Phase I work and demonstrated utility in measuring engagement and meaningfully refining our implementation efforts.

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
	completed to document how our team engages with the CSAB members. Partner engagement surveys will be administered and analyzed after each meeting.	
Secondary		
Our secondary objective is to implement and evaluate the impact of our innovative, multilevel, and multicomponent implementation strategy bundle to optimize COVID-19 rapid testing among underserved, Latino communities using a roll-out implementation optimization study design across four clinics over 18 months.	<p>Refer to Figure 1 in Schema 1.2. We will roll out 3 strategies to optimize COVID-19 testing: 1. current, walk-up free testing.</p> <p>2. promotores-led COVID-19 test counseling, and preventive care reminders.</p> <p>3. vending machines that dispense FDA-authorized self-testing kits.</p> <p>For each strategy, participants will consent into the study, provide demographics and test history, and receive a free rapid antigen test (RAT) kit. After receiving their test kit, participants will be prompted to return their results and fill out a survey about their COVID-19 experiences. Study subjects will be contacted up to three times over a course of 4 weeks to return their results and complete the survey. Study coordinators will use participants' preferred method of contact.</p> <p>The vending machines will be placed in 4 SYH clinics throughout South San Diego over four cycles of preparation after refinements to the implementation strategy bundle listed above.</p> <p>We will also conduct a total of 60 interviews with patients/ community members (15 per clinic and targeting to include 5 interviews/ clinic with caregivers or adolescents). Patients/ community members will be identified for interviews based on their interest expressed when initially obtaining tests. An additional set of interviews will be conducted with a total of 12 providers/ staff (3/clinic). Providers/ staff will be</p>	Both quantitative survey and qualitative interview data are necessary to comprehensively and accurately evaluate the impact of our implementation efforts.

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
	identified on their involvement in supporting the implementation guides or having exposure to the multicomponent implementation strategy bundle. Separate semi-structured interview guides will be developed, and pilot tested for clinic providers/staff and patients/community members (Spanish and English) and will be guided by the PRISM domains. Interviews will be 45-60 minutes, audio-recorded, and transcribed. All interview participants will receive \$40 for their time.	

4 STUDY DESIGN

4.1 OVERALL DESIGN

- A statement of the hypothesis
 - We hypothesize that refining, implementing, and testing a multicomponent implementation strategy to optimize FDA-approved rapid antigen testing will reduce testing and health disparities for underserved communities.
- Phase of the trial, if applicable
 - Not applicable
- A description of the type/design of trial to be conducted (e.g., randomized, placebo-controlled, double-blinded, parallel design, open-label, dose escalation, dose-ranging, adaptive, cluster randomized, group sequential, multi-regional, superiority or non-inferiority design)
 - This is a roll-out implementation optimization clinical trial. Four cycles of preparation, initial roll-out, and sustainment will be launched across 21 months, across four clinic sites.
- A description of methods to be used to minimize bias
 - Drs. Laurent, Stadnick, and Rabin will work closely to manage any potential missing data issues, to measure and correct potential biases, and for administrative and fiscal oversight.
- Dose escalation or dose-ranging details should be contained in **Section 6.1.2, Dosing and Administration**
 - Not applicable
- The number of study groups/arms and study intervention duration

- For the CSAB (Aim 1), a total of up to 18 members will be included. The CSAB will include: up to 6 community members (who may also be SYH patients) from the four areas from which we will conduct patient recruitment (San Ysidro, Chula Vista, Lincoln Park, Logan Heights), up to 6 clinical providers or administrators from SYH, up to 3 public health research partners, up to 2 policy partners, and 1 County of San Diego Health and Human Services partner. The CSAB members will be recruited to ensure a well-balanced board of community members who reside near the SYH clinics where the study is conducted, SYH clinic administrators and providers, and public health professionals. The members will be recruited through existing relationships with the research, community, and clinical partners of the study. This CSAB will focus on the refinement and evaluation of the COVID-19 testing strategies. These individuals will comprise Cohort 1.
- For Aim 2, individuals ages 2 and above will be included in this study, for the remainder of the study. Study enrollment will occur at San Ysidro Health (SYH) Clinics. SYH and UCSD research staff actively recruit any eligible individual who approaches the clinic. Research members will also promote on social media and distribute flyers at local businesses. Aim 2 will have 2 cohorts:
 - Cohort 2: Community members, SYH patients and non-patients (n= 7,500)
 - Cohort 3: SYH providers and staff (n= 12)
- Indicate if single site or multi-site
 - Multi-site working with San Ysidro Health Centers. Locations are San Ysidro Health Center, Ocean View Health Center, King Chavez Health Center, Chula Vista Medical Plaza.
- Name of study intervention(s)
 - Rapid antigen testing, vending machines that dispense testing kits, promotor-led health navigation, and testing support, walk-up testing.
- Note if interim analysis is planned and refer to details in **Section 9.4.6, Planned Interim Analysis**
 - Not applicable
- Note if the study includes any stratifications and if so, identify the stratification planned (e.g. sex, race/ethnicity, age, dose) and refer to details in **Section 9.4.7, Sub-Group Analyses**
 - Primary endpoint analysis will include only aggregated data. Additional analysis to understand patterns and characteristics of testing uptake, exposures, and symptoms and to guide adaptive implementation will be conducted among sub-groups of participants, including clinic site, age group, sex, and race/ethnicity.
- Name of sub-studies, if any, included in this protocol
 - A subset of participants will be selected from each clinical site to provide feedback on the implementation through a recorded interview. These participants will be consented separately using the information sheet.
- Research Staff Members
 - A complete list of research staff members will be included in Study Contact Form. Key personnel include UC San Diego research team and SYH research team.

- The CO-CREATE project offers an internship through the department of public health at UCSD (FMPH400) which allows students interns to gain research experience. These students will be trained by UCSD research staff and complete all CITI trainings (HIPAA, GCP, and Biomedical Research).
- The Global ARC is an organization that will help organize the CSAB meetings and recruit community members. The Global ARC members are valuable to the project, however they will not be involved in the research consenting/data collection process.
- All research staff involved in consenting and working with participants are bilingual in Spanish and English. UCSD research staff were hired under the Bilingual Clinical Research Coordinator job description. San Ysidro Health interviewed all candidate in Spanish and hired staff that were fluent in Spanish/English. All UCSD student interns were interviewed in Spanish and English to prove fluency to work with research participants.
- Informed Consent Process
 - Aim 1
 - UCSD research staff will obtain informed consent from members of the Community and Scientific Advisory Board using the exempt information sheet. Consent will be obtained over virtual Zoom calls. This consent requests a waiver of documented consent as the meetings will be conducted over zoom and the study present no more than minimal risk to the participant. Aim 1 of CO-CREATE-Ex project is considered exempt category 2: research involving the use of survey procedures and interview procedures, where information obtained will be recorded in a manner that the subject cannot be identified and disclosure of the subjects' responses outside of the research could not reasonably place the subject at risk.
 - The CSAB information sheet consent has been translated by NIH RADx-UP Coordination and Data Collection Center (CDCC) with a second review by San Ysidro Health Bilingual Research Staff. Certificates of Translation and Attestation have been uploaded into Kuali. Spanish versions of consent will be uploaded in amendment after approval of English consents.
 - Aim 2
 - Testing Implementation
 - Informed consent documents are available for adults, parents, adolescents ages 13-17, and children ages 7-12. Each consent has been translated by NIH RADx-UP Coordination and Data Collection Center (CDCC) with a second review by San Ysidro Health Bilingual Research Staff. Certificates of Translation and Attestation have been uploaded into Kuali. Spanish versions of consent will be uploaded in amendment after approval of English consents.
 - All participants who wish to enroll in the CO-CREATE-Ex implementation strategies will be required to provide their electronic consent using the web-based link or scanning a QR code. The landing page will show the

consent form that corresponds to the participants age group (adult, parental, adolescent or child). The participant will read through the consent form and download a copy prior to selecting “Yes” or “No” to participate. After indicating their response, the date will auto-stamp to date consent was taken and the participant will sign their name using the electronic signature feature on REDCAP.

- For any participants that have difficulty accessing the web-based link and/or QR code, a study staff member will be available to assist with the consent/registration process. Participants may approach a study staff member (either UCSD or SYH) at the testing site or contact a UCSD study staff member by calling the UCSD study phone. The study staff member can guide the participant through the consent form and help take electronic consent of the participant. The consent form and bill of rights can be emailed to the participant or the participant may request a paper copy for their records.
- Interviews
 - UCSD research staff will use the exempt information sheet to obtain informed consent from clinic providers, staff, patients or community members prior to conducting the interview. This consent requests a waiver of documented consent as the interviews will be conducted over zoom and the study and questions present no more than minimal risk to the participant. Aim 2 interviews of CO-CREATE-Ex project is considered exempt category 2: research involving the use of survey procedures and interview procedures, where information obtained will be recorded in a manner that the subject cannot be identified and disclosure of the subjects’ responses outside of the research could not reasonably place the subject at risk.
 - The Aim 2 Interview information sheet consent are translated by NIH RADx-UP Coordination and Data Collection Center (CDCC) with a second review by San Ysidro Health Bilingual Research Staff. Certificates of Translation and Attestation have been uploaded into Kuali. Spanish versions of consent will be uploaded in amendment after approval of English consents.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

We chose a roll-out implementation optimization (ROIO) design to implement our study. This is a novel implementation science study design that affords a balance of rigor and flexibility to refine in response rapidly and iteratively to dynamic contexts like the pandemic. Prior to a testing strategy being rolled out, clinic sites will be providing their standard of care (control group).

4.3 JUSTIFICATION FOR DOSE

Not Applicable

4.4 END OF STUDY DEFINITION

The duration of the study is 2 years. Participants are allowed to return to vending machines and walk-up testing sites to test as needed for the entire duration of the study. Participants will be notified when the project will end so that they may plan their visits accordingly.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria for their respective cohort:

Cohort 1 Community and Scientific Advisory Board:

1. Age 18 years or older
2. Speak Spanish or English

Cohort 2 Testing Group:

1. Speak Spanish and/or English.
2. Affiliated with San Ysidro Health as a patient at select clinics (San Ysidro, Chula Vista, Lincoln Park, and Logan Heights) OR
3. A member of a community near a SYH clinic (San Ysidro, Chula Vista, Lincoln Park, and Logan Heights).
4. Ages 2 and older (for use of FDA-authorized antigen test kits)

Cohort 3 Healthcare Providers/Staff/Administrators:

1. Speaks Spanish and/or English.
2. Employed as a SYH clinical provider, administrator, or clinical staff member at a participating clinic

For Cohort 2 Testing Group

The populations we propose to focus on have been disproportionately impacted by COVID-19. For example, the San Ysidro zip code (92173) has the highest confirmed COVID-19 case rate per 100,000 population (48,219), and the adjacent zip code (92154) has the second highest (38,758); in comparison, the average for San Diego City is 20,459. The case rates for the zip codes where the proposed new clinic sites are located are the next three highest in the County: 35,715 (Ocean View clinic in zip code 92133); 34,209 (King Chavez Medical Center in zip code 92114); and 31,623 (Chula Vista Medical Plaza in zip code 91911).

In addition to a high case rate, these areas have a high percentage of children and adolescents (median age 32.2 years); individuals living overcrowded housing; and individuals who are migrants/immigrants (in zip code 92173, 24.5% are US citizens who are not US born, and 24.0% are not US citizens) and communities with high pollution burdens.

Additionally, because children have been considered at lower risk of severe disease, testing in this population has been lacking and repeated testing in a high burden setting will increase our understanding of transmission and transmission patterns in communities with limited access to health care services. We will include children ages 2 and up to use the antigen test kits.

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Institutionalization for psychiatric disorder, developmental delay, or criminal activity.
2. Unable to provide informed consent.

3. Participant is under the age of 2 years old for antigen test kit use.

5.3 LIFESTYLE CONSIDERATIONS

Not Applicable

5.4 SCREEN FAILURES

Participants who are unable to register at the vending machine will have the opportunity to register with a study staff member on-site or by calling the study phone number. If a participant is unable to register with a study staff member due to developmental delay, they will be excluded and alternative resources to receive free rapid antigen test kits will be offered to them at that time.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

Our study has 2 Aims: Aim 1 is focused on preparing for the intervention using the CSAB members and Aim 2 is the study intervention. We will describe both aims here with an emphasis on Aim 2 activities.

Aim 1: To refine and operationalize our multi-component implementation strategy bundle and a related set of outcome metrics for FDA-authorized COVID-19 rapid testing.

- The CSAB members will be recruited to ensure a well-balanced board of community members who reside near the SYH clinics where the study is conducted, SYH clinic administrators and providers, and public health professionals. The perspectives of these groups are considered essential to the design, planning, and execution of the research activities. The members will be recruited through existing relationships with the research, community, and clinical partners of the study.
- Using our partnership with the Global ARC and Community and Scientific Advisory Board, we will finalize and operationalize the implementation strategy bundle and measures of implementation and sustainment success within the first quarter.
- CSAB members will be provided with \$100 per meeting and a total of 10 CSAB meetings will be held across the 2 years of the project. Each session will be recorded and structured forms will be completed to document how our team engages with the CSAB members.
- Partner engagement surveys will be administered and analyzed after each meeting.
 - Engagement surveys were used in another COVID-19 study (protocol: 201795) conducted by Nicole Stadnick and Borsika Rabin. Translation of this survey was done by David de los Reyes, certificate of this is uploaded in Kualu.

Aim 2: To implement and evaluate the impact of our innovative, multilevel, and multicomponent implementation strategy bundle to optimize COVID-19 rapid testing among underserved, Latino communities in Central and South San Diego using a ROIO study design across 4 clinics over 18 months.

- Our community-driven research project will be guided by the Practical, Robust Implementation and Sustainment Model (PRISM) for roll-out preparation, iterative refinement and evaluation

activities. PRISM Fit Assessment will involve completion of a 21-item survey by various members including: 2-3 SYH clinic staff, promotores, and 1 clinic operational leader from Clinic 1.

- This will be repeated for each clinic and again at the end of the study.
- The PRISM fit assessment will be uploaded with study materials in Quali.
- Implementation strategies include:
 - Walk-up on-site testing
 - Promotore-led testing navigation and general preventive care reminders.
 - No-cost self-testing kit vending machines.

Four SYH clinics will be targeted for inclusion to enroll up to 7,500 participants. The San Ysidro Health center (SYHC) will be the main clinic for this study. The other clinics will be Chula Vista (CVMP), King Chavez in Lincoln park (KCHC), and Ocean View (OV) in Logan Heights. SYHC will not be randomized because it is currently an active intervention site. The other 3 clinics CVMP, KCHC, and OV will be randomized to the start of the implementation strategy bundle rollout. Clinic randomization will occur using the random number generator function in Excel. SYH and UCSD research staff actively recruit any who approaches the clinic. Research members will also promote on social media and flyer at local businesses.

We estimate capacity to distribute 52,000 FDA-authorized rapid tests that will be provided to the research team by the San Diego County Health and Human Services and California Department of Public Health.

Data and assay results will be used for both clinical and research purposes. All collected data used for research will use codes rather than subject names. Only the PIs, clinicians and primary research team members will have access to participant identifiers. We will use a data entry, training and management system, UCSD's Sharepoint system complies with the data security requirements of HIPAA and the HITECH Act. All key research staff and investigators will complete extensive training on data collection, management and protection and will meet at least quarterly to discuss issues and procedures.

Aim 2 Testing plan of study activities is outlined below:

1. Data collection will start at San Ysidro Health Center – Main Clinic (SYHC). Walk-up testing will continue from phase 1 (CO-CREATE) and be complemented by promotore-led education and a vending machine.
 - a. SYH research staff, promotores, and UCSD research staff will lead recruitment efforts in front and inside the SYH clinic. Recruitment flyers will be posted at businesses surrounding the community. The research project social media will include CDC health recommendations and recruitment flyer to boost recruitment efforts.
 - b. Participants will be asked to consent into the research study by scanning a QR code on the vending machine, engaging with study staff members/promotores on-site, or through a web-based landing page. Parental consent will be prompted for children under 18 years, separate consents will be populated in redcap for children ages 13-17 and ages 7-12. Any children ages 2-6 years old will only require parental consent. After reading through the consent form participants will select yes to participate or no to participate.
 - i. The landing page link: <https://mm214.com/ucsdapp/>
 1. **This link will be changed once IT security permissions are granted, research team will update in an amendment. QR code has not been created yet, will submit in an amendment.**
 - ii. If selected yes, participants will be asked to provide their demographic information: name, date of birth, phone number, address, email address,

- race/ethnicity, gender as well as information about their symptoms, vaccine status and testing history.
1. Parents will fill out demographics of the child participating. If multiple children are being enrolled, the parent will be asked to fill out a consent and register each child as a research participant.
- iii. If selected no, participants will be offered a page of resources to access alternative test kits.
 1. **List of resources pending. Study team is waiting for list from SYH, will submit list of resources in amendment.**
 - c. After consent and registration, participants will be provided a code to enter into the vending machine to dispense their antigen test kit.
 1. Only one code will be provided to each participant. For example: for a family of 4, each member will have their own code to use at the vending machine.
 - d. Participants will be prompted to leave the vending machine and return home to take their test. After which the study team will send out a REDCap link for the participant to report their test results.
 - i. The study team will attempt to collect these test results up to 3 times after the participant receives the test kit. After the 3rd attempt, if no response is received, the study team will not send out additional notices.
 - ii. **Link for reporting results is pending, will submit once developed in an amendment**
 - e. Participants will also be invited to complete comprehensive data collection surveys for capture of required common data elements (CDEs) through REDCap.
 - i. Web-survey data kept by the research project will be coded with a unique identifying number for which the key will be separately stored and limited to primary research staff members who will only share this data to the extent necessary for required reporting purposes.
 - ii. Participants may complete this survey via email, text, or paper, preferences will be collected at registration.
 - iii. All CDE questions and translations for the survey are provided by NIH's RADx-UP
 1. <https://radx-up.org/research/cdes/>
 2. Data dictionaries for the survey questions in English and Spanish are uploaded in Kuali.
 - iv. This data will be batch transferred to RADx-UP at required frequencies. *
 - f. Participants may return to the vending machine to receive additional test kits as needed throughout the study. The protocol remains mostly the same. Return participants do not need to re-consent unless there is an amendment to the consent form. Return participants will be asked to report symptoms and any changes to testing and vaccine history prior to receiving another code.
 - i. Return participants will be asked to complete another comprehensive data collection survey for capture of required common data elements (CDEs) through REDCap. This return survey will be much shorter than the initial survey. The questions for the return survey are pulled from the initial questions. The return survey should only take 5-10 minutes to complete.
 - g. If results are reported back to the study team, additional guidance will be provided to the participants as to when they should repeat their test. These guidelines are derived

- directly from the Center for Disease Control (CDC) and California Department of Public Health (CDPH). The guidelines will be updated throughout the study.
- h. No compensation will be given for receiving a test kit or completing the survey.
2. The vending machine protocol will be the same for the other 3 clinical sites except without the walk-up testing site.
- a. For clinics in Lincoln Park, Logan Heights and Chula Vista, vending machines and promotores will be available for participants to access.
 - i. Promotores will provide the study staff support with recruitment and enrollment as well as health education around COVID-19.
 - b. Walk-up testing will only be available at San Ysidro Health Centers Main Clinic with limited hours.
 - i. Study staff will be available to help participants verbally consent and register to receive an antigen test kit. Study staff will be available to provide support with filling out the survey or completing the test kit. If results are returned to study staff, additional guidance will be provided from CDPH and CDC.
 - ii. No walk-up testing will be available at clinics in Lincoln Park, Logan Heights or Chula Vista.
3. Qualitative interviews with patients/community members and clinic providers/staff will be conducted after each initial roll-out period (after 3 months of implementation) to understand their experiences with the multicomponent implementation strategy bundle and identify potential areas for improvement. ***We note that the interview guides for these interactions are being developed in partnership with our CSAB, and will be submitted for review and receive IRB approval prior to use***
- a. We will conduct a total of **60** interviews with patients/community members and **12** interviews with providers/staff.
 - i. 15 patient/community members interviews per clinic and targeting to include 5 interviews per clinic with caregivers and adolescents.
 - ii. 3 provider/staff interviews per clinic
 - iii. Interview guides will be drafted and developed after the initial CSAB sessions.
 - b. Patients/community members will be identified for interviews based on their interest expressed when initially obtaining tests as part of the walk-up onsite clinic or vending machine. We will select a combination of participants from both testing sources and both adult and caregiver/adolescent participants.
 - c. Providers/staff will be identified based on their involvement in supporting the implementation or having exposure to the multicomponent implementation strategy bundle.
 - d. Separate semi-structured interview guides will be developed and pilot tested for clinic providers/staff and patients/community members in English and Spanish.
 - i. Interview guides will be drafted and developed after initial CSAB sessions.
 - e. Interviews will be 45-60 minutes, audio-recorded and transcribed.
 - i. Audio consent will be collected prior to recording. No video will be saved, only audio recording.
 - ii. Audio recording data from interviews will be uploaded by study staff securely to the HIPPA compliant file sharing Sharepoint site. Audio data will also be coded with a unique identifying number for all participants.
 - iii. Qualitative interview data will be de-identified and transcribed by study personnel or HIPPA compliant transcription services.
 - f. All interview participants will receive \$40 for their time.

- g. Rapid matrix analysis of patient/community member and provider/staff interviews and periodic reflections will be conducted to identify key concerns and opportunities for refinements. This information will be summarized and presented to the CSAB so that refinements can be identified and changes can be made to the strategy bundle.

*Data use agreement with Duke University and UC San Diego pending.

6.1.2 DOSING AND ADMINISTRATION

Not Applicable

6.2 PREPARATION/HANDLING/STORAGE/ACCOUNTABILITY

6.2.1 ACQUISITION AND ACCOUNTABILITY

Not Applicable

6.2.2 FORMULATION, APPEARANCE, PACKAGING, AND LABELING

Not Applicable

6.2.3 PRODUCT STORAGE AND STABILITY

The COVID-19 Rapid Antigen Test (RAT) kits will be stored at UC San Diego's Biomedical Science Building. Test kits will be stored in a locked cabinet located on the 5th floor, only study staff personnel will have badge access to this building and code access to the cabinet. Test kits will be stored in a dry location between 36-86°F. <https://www.fda.gov/media/153923/download>

The outdoor vending machines will be temperature-controlled to preserve the RAT kits.

6.2.4 PREPARATION

The Community and Scientific Advisory Board will be identified and invited by MPIs Dr. Stadnick and Dr. Rabin, and Community Partners from the Global Action Research Center.

Vending Machines will be ordered by the study staff through Intelligent Dispensing Solutions.

Test kits will be ordered through the California Department of Public Health (CDPH).

Promotores will be hired by San Ysidro Health Centers and managed by the SYH research staff.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

For this phased implementation study our first clinic site will be located where our previous testing program originated to reduce interruption to COVID-10 testing access. However, in order to reduce bias in the continuing clinic site selection, we will randomize the implementation order for the remaining participating clinical sites. There will be no blinding of participants or investigators to the study intervention of providing COVID-19 RATs.

6.4 STUDY INTERVENTION COMPLIANCE

Not Applicable

6.5 CONCOMITANT THERAPY

Not Applicable

6.5.1 RESCUE MEDICINE

Not Applicable

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

Participants will be allowed to stop participation at any time by contacting one of the study staff members or PI. The PI may remove a participant from the study if they find this to be in their best interest.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Significant study intervention non-compliance
- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant.
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to respond to survey or input their test results and is unable to be contacted by the study site staff.

No action will be taken if the participants fail to respond to study site staff. Staff members will attempt to contact participants up to 3 times via text, phone call, email or, if necessary, a certified letter to the participants' last known mailing address, after receiving their test kits over a period of 4 weeks. If by then the participant does not respond, the study staff will cease contact.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 EFFICACY ASSESSMENTS

Not Applicable.

8.2 SAFETY AND OTHER ASSESSMENTS

Not Applicable

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

The FDA definition of an Adverse event is any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

An adverse event (AE) or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse. The only SAE relevant to participants is the potential loss of confidentiality.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

All adverse events (AEs) must have their relationship to study intervention assessed by the PI who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
- **Not Related** – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

The PI will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

The Data Safety and Monitoring Board will be apprised of all AEs within 7 days of occurrence, and will review and provide guidance on resolution of all AEs.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and during an interview of a study participant.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, PI's assessment of severity, relationship to study intervention (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

All adverse events including serious adverse events will be reported to the UCSD Human Research Protections Program and the assigned Program Officer at the NIH within 7 days of the event occurring.

8.3.5 ADVERSE EVENT REPORTING

All adverse events will be reviewed by the MPIs (Drs. Laurent, Stadnick, Rabin) and reported to the UCSD Human Research Protections Program and the assigned Program Officer at the relevant NIH institute within 7 days of the occurrence and summarized in the annual progress report. Such adverse events include but are not limited to:

1. Need to break confidentiality to report criminal (e.g. child maltreatment) behavior of a provider;
2. Inadvertent harm related to participation in the study such as disclosing health diagnoses of participants;
3. Significant clinical deterioration as defined as a need for hospitalization;
4. Loss of data related to the trial for any reason.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

Study staff will use the same protocol listed in section 8.3.5.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

Not Applicable

8.3.8 EVENTS OF SPECIAL INTEREST

Not Applicable

8.3.9 REPORTING OF PREGNANCY

Not applicable

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS (UP)

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research (“possibly related” means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEM REPORTING

The study staff will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI’s name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP.
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and to the study sponsor within 7 days of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and to the DCC/study sponsor within 7 days of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within 7 days of the IRB's receipt of the report of the problem from the investigator.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Not applicable

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Efficacy Endpoint(s): the increased distribution of rapid antigen tests within our target communities, measured using a proxy outcome, the proportion of clinic patients visits to the number of rapid antigen kits distributed per month at each participating clinic. We anticipate an increased distribution to approximately 40% of clinic patients per month which would result in the distribution of 1,822 kits per month during the final treatment sequence.

Null hypothesis: At the completion of the study the ratio of rapid antigen kits distributed to the number of clinic patient visits per month will be less than 40%.

Alternative hypothesis: At the completion of the study the ratio of rapid antigen kits distributed to the number of clinic patient visits per month will be equal to or greater than 40%.

- Secondary Efficacy Endpoint(s):

9.2 SAMPLE SIZE DETERMINATION

Sample size and power. The number of participating clusters/clinics and target clinic participant enrollment for our ROIO study design was determined using cluster randomized trial sample size estimation tools. Per the ROIO study design, each clinic cluster will begin in the control group and then cross over into the intervention group at different time points and then continue with the intervention until the end of the study (see **Figure 1**). Although we anticipate the implementation strategies as outlined by CSAB will undergo some adjustments during the implementation process, the target cluster/clinic sample size estimates are based on a stepped wedge design using serial cross-sectional evaluations of EHR and test kits distributed.

V1	V2	V3	V4	V5
0	1	1	1	1
0	0	1	1	1
0	0	0	1	1
0	0	0	0	1

Figure 1. Design matrix structure: one cluster per

Our primary outcome, the increased distribution of rapid antigen tests within our target communities, will be measured using a proxy outcome, the proportion of clinic patients visits to the number of rapid antigen kits distributed per month at each participating clinic. Currently, rapid antigen test kit distribution among target clinic patients ranges from about 7 to 13% with approximately 430 kits being distributed per month between all four clinics. We aim to increase distribution to equal approximate distribution of test kits to 40% of clinic patients per month which would result in the distribution of 1,822 kits per months during the final treatment sequence resulting in a total distribution of 23,236 tests to clinic patients over the course of the study. Based on data collected from our previous PCR based testing intervention, approximately 40% of testing uptake occurred among clinic patients and the remaining 60% from community members even when the intervention was clinic based. We anticipate a similar community uptake during this study resulting in a total uptake of 58,091 test kits over the course of the study.

Using the Shiny CRT Calculator, (<https://clusterrcts.shinyapps.io/rshinyapp/>) we determined that given an average minimum cluster sample size of 285 across 4 clinics we will have sufficient power ($\beta > 0.8$) to determine an intervention proportion increase of 0.07 to 0.4 assuming the following: stepped-wedge design, cross-sectional sampling structure at each of 4 sequences (approximately every three months in our study), 0.5 coefficient of variation in cluster sizes (based on average number of patient encounters per month per clinic), intra-cluster correlation (ICC) of 0.02, for our binary outcome (test or no-test). We also assumed exchangeable cluster correlation structure as SARS-CoV-2 testing demand has been impacted significantly with changes in variant severity and transmissibility.

9.3 POPULATIONS FOR ANALYSES

Primary outcome dataset will consist of the aggregated total person clinic visits at each clinic site (extracted from clinic EHR) and total number of test kits distributed (extracted from REDCap).

We will also evaluate other populations for feedback on process and non-primary outcome data analysis. These populations include the include the community and scientific advisory board members, community members, SYH patients and non-patients, and SYH providers, administrators, and staff as described below:

Qualitative analysis:

Group 1: Community and scientific advisory board members

- We plan to enroll up to 18 participants to join the CSAB.

Group 2: Community members, SYH patients and non-patients

- We plan to recruit and enroll up to 7,500 participants, and among those we plan to recruit, screen and invite a sub-set of 60 participants to participate in a 45-60 minute virtual interview.

Group 3: SYH providers, administrators, and staff

- We plan to recruit and enroll up to 12 SYH providers, administrators and staff to participate in a 45–60-minute virtual interview.

Quantitative analysis:

Group 2: Community members, SYH patients and non-patients

- We plan to recruit and enroll up to 7,500 participants.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Quantitative Data Analysis. Quantitative data from study databases and participants will be summarized using simple descriptive statistics including frequencies, measures of central tendency, and variability along with data visualization methods, such as frequency tables, bar charts, line graphs, and scatter plots to understand patterns and characteristics of testing uptake, exposures, and symptoms and to guide adaptive implementation. In order to account for potential within-clinic correlation we will reduce data for each cluster to a single observation, and then carry out standard two-sample analyses to evaluate our primary hypothesis. Additionally, we will also analyze the data on an individual level using parametric and non-parametric tests to compare the survey responses between the adaptive arms of the trial while controlling for a variety of demographic and socioeconomic variables, including the SYH clinic cluster. We will use hierarchical multilevel models to ensure the inclusion of random effects, variation between clusters (clinic sites), variation between times within clusters, and the fixed effect of time which will be estimated independently of treatment effect so that secular changes over time will not be mistaken for effect of treatment. This is key, based on significant variations in PCR testing uptake observed during previous COVID-19 variant waves. We will conduct additional analyses to determine the appropriateness of the test type distribution within the context of symptom onset and/or exposure time frame.

Data analysis and rapid iterative refinement cycle. Qualitative interviews with patients/community members and clinic providers/staff will be conducted after each initial roll-out period (after 3 months of implementation) to understand their experiences with the multicomponent implementation strategy bundle and identify potential areas for improvement. We will conduct a total of 60 interviews with patients/community members (15/clinic and targeting to include 5 interviews/clinic with caregivers or adolescents). Patients/community members will be identified for interviews based on their interest expressed when initially obtaining tests as part of the walk-in onsite clinic or vending machine. We will select a combination of participants from both testing sources and both adult and caregiver/adolescent participants. An additional set of interviews will be conducted with a total of 12 providers/staff (3/clinic). Providers/staff will be identified based on their involvement in supporting the implementation or having exposure to the multicomponent implementation strategy bundle.

Rapid matrix analysis of patient/community member and provider/staff interviews and periodic reflections will be conducted to identify key concerns and opportunities for refinements. This information along with data about the implementation of the strategy bundle and testing results will be summarized and presented to the CSAB (two sessions after Clinic 1 roll-out and one session after each consecutive clinic roll-out). A list of possible refinements will be identified based on input from the CSAB and final decisions about refinements will be made by the UCSD, SYH, and Global ARC teams. Any

changes made to the strategy bundle and procedures will be documented in the Adaptation documentation database. After refinements to the multicomponent strategy bundle have been completed, the PRISM Fit Assessment will be conducted with the next clinic (**see description in Aim 1**) to allow for clinic-specific further adjustments. A matrix approach will be used to triangulate data from quantitative and qualitative sources using the key domains of PRISM. A joint display will also be produced to support the integration of data sources.

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

In order to account for potential within-clinic correlation we will reduce data for each cluster to a single observation, and then carry out standard two-sample analyses to evaluate our primary hypothesis.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

No prespecified secondary outcomes.

9.4.4 SAFETY ANALYSES

Not Applicable

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Quantitative data from study databases and participants will be summarized using simple descriptive statistics including frequencies, measures of central tendency, and variability along with data visualization methods, such as frequency tables, bar charts, line graphs, and scatter plots to understand patterns and characteristics of testing uptake, exposures, and symptoms and to guide adaptive implementation.

9.4.6 PLANNED INTERIM ANALYSES

Not applicable.

9.4.7 SUB-GROUP ANALYSES

Primary endpoint analysis will include only aggregated data. Additional analysis to understand patterns and characteristics of testing uptake, exposures, and symptoms and to guide adaptive implementation will be conducted among sub-groups of participants, including clinic site, age group, sex, and race/ethnicity.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Participant data will be captured and stored for each individual for each measure at each timepoint.

9.4.9 EXPLORATORY ANALYSES

Not applicable

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes.

10.1.2 CONFIDENTIALITY AND PRIVACY

The current research proposes to collect (a) minimal personally identifying data (e.g., name, birth date, ethnicity, etc.) and (b) research data (e.g., questionnaires and outcome measures, extracted de-identified health records). When connected only to a numeric identifier, the majority of the research data does not contain information that could identify a participant. When possible, standard protocols containing a numeric research identifier will be employed to separate personally identifying information from the research data. All audio data will be recorded in a digital format on encrypted audio recording devices, labeled using ID numbers only and stored on HIPAA-compliant cloud-based storage (Sharepoint). Study staff will collect audio recordings from encrypted audio recording devices and upload them to a HIPAA compliant cloud-based storage (Sharepoint). These procedures are very similar to procedures used in our other approved research projects at our centers and as such, the investigators have had substantial experience ensuring the safety and confidentiality of audio data. Personal identifying information will be stored in a single database that is managed by the consortium data reporting unit. This database will be encrypted and have an access password that is only known to the PI and appropriate research members. All computer screens will have a five-minute time limit that will produce a blank screen if left unattended and will require a password to re-access the screen. This database will only be available to the project team. The consortium data reporting unit has experience storing confidential information for multiple research projects, thus maintains stringent security measures. Research data collected will be coded with a participant's unique identifier, or number. Personal identifying data will not appear on any research data. All individuals working on the study will sign confidentiality agreements to never disclose any individual information regarding any aspect of the study. As it true for all UCSD personnel, any person(s) working on this research project will have undergone extensive orientation and training on issues regarding the maintenance and protection of confidentiality (e.g., sending confidential material to a community printer, using names while conducting phone interviews, etc.).

Data transfer. We have an established process to maintain compliance with the NIH requirement that all studies funded under this RFA actively coordinate, collaborate, and share all project data with the RADx-UP Coordination and Data Collection Center (CDCC). Currently our Data Reporting Unit transmits survey and study data to CDCC and will continue this transfer process of weekly transmission of RADx-UP common data elements (CDEs) and quarterly submission of all other project data. The CO-CREATE-Ex Data Use Agreement has been submitted through Kualu and is pending approval.

All data collected in the survey, except for name, date of birth, address, and contact information will be submitted to RADx-UPhome, the RADx-UP program's data portal, as required by the funding agency (NIH). This will include responses entered into free-text fields.

Developed and managed by Duke, myRADx-UPhome is a secure web portal through which designated individuals from each RADx-UP project can upload study data to the CDCC and view the data quality reports for each upload. These reports provide feedback on the conformance of the Project's file with the RADx-UP codebook/expected content and file structure. myRADx-UPhome also provides designated users from each project access to non-data related collaboration features such as resource libraries and project/user directories.

myRADx-UPhome supports federated authentication which allows users from projects to login with their organizational credentials. Organizations must be part of the InCommon Federation to be supported. For users from organizations that are not supported, Duke accounts are provisioned.

Authorization to access functions within myRADx-UPhome is managed by the RADx-UP CDCC team. Only individuals designated by the Principal Investigators on each project are assigned appropriate roles to enforce access control. For example, access to the data upload function and consequent data quality reports is limited to the designated data managers for each project.

A subscription within the Duke owned/maintained Microsoft Azure tenant is dedicated to RADx-UP. Data uploaded by the projects is stored within this RADx-UP subscription and does not persist in the portal. The RADx-UP subscription is secured using Duke standard procedures in addition to using Microsoft's standard security blueprints that provide foundational security controls for the infrastructure. These security controls include RBAC settings at a management group, subscription and resource group level, the use of Azure Defender for SQL and Storage, the use of Azure Security Center and Azure Sentinel and the use of policy initiatives for HIPAA/HITRUST and NIST 800-171 and NIST 800-53.

This data will be available to members of the RADx-UP consortium, who have the appropriate Data Use Agreements in place allowing access to both structured and free text data; the exception will be for structured fields with fewer than 11 responses.

From RADx-UPhome, the dataset will be further stripped of free text responses before transmission to the RADxHUB, which is the overall RADx program's data repository.

In Summary:

- No dashboards will show data in free text fields.
- Statistical datasets are provided for further research.
 - Below is a summary of how the free text entries in the CDE are used in/for analyses:
 - Anyone working on RADx-UP cross-consortium manuscripts have the appropriate data agreements in place to see these free text data, so all writing teams will have access to them.
 - Duke will not report any aggregate data with cell sizes below 11, and Duke will not perform any analyses with small sample sizes.
- Duke will also use the text entries to derive additional categories of interest for an analysis

The following language will be included in the consent forms: "Your data, that does not contain your name or other information that could easily identify you, will be combined with data from the other

people who take part in the RADx-UP program. Researchers will use the data to learn more about COVID-19 or other diseases and conditions. The Duke Clinical Research Institute is a research group chosen by the NIH to combine the data collected from everyone taking part in RADx-UP studies.”

Certificate of Confidentiality

To further protect the privacy of study participants, a Certificate of Confidentiality will be issued by the National Institutes of Health (NIH). This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to participants.

10.1.3 FUTURE USE OF STORED SPECIMENS AND DATA

The sources of data for this study will include:

1. COVID-19 testing and epidemiological data.
2. Online or paper-based survey data from participants for required common data elements (CDEs)
3. Online survey data from CSAB members about stakeholder engagement during CSAB meetings
4. Interviews with promotores, SYH clinic providers, administrators, and staff, and patients
5. Ethnographic data collected during CSAB meetings on stakeholder interactions.
6. Study subject demographics (race/ethnicity, self-reported gender, symptoms, exposure, age)

Data collected for this study will be analyzed and stored at the UC San Diego Altman Clinical and Translational Research Institute (ACTRI) using a secure online survey program software, REDCap. We will collect identifiable information as well as the RADx-UP common data elements (CDEs). The CDEs collected from the surveys will be transmitted to Duke Clinical Research Institute to be shared with the RADx-UP Coordination and Data Collection Center (CDCC). All CDE questions and translations for the survey are provided by NIH RADx-UP project: <https://radx-up.org/research/cdes/>. Our data reporting unit will transmit RADx-UP CDEs to the CDCC weekly and will transmit all other project data quarterly. Data Use Agreement from Duke has been submitted through Kualu and is pending.

Qualitative interview data will be de-identified and transcribed by study personnel or HIPPA compliant transcription services. Audio recording data from interviews will be uploaded by study staff securely to the HIPPA compliant file sharing Sharepoint sites. Audio data will also be coded with a unique identifying number for all participants.

After the study is completed, the de-identified, archived data will be transmitted to and stored in the RADx-UPhome and RADxHUB data repositories, as noted in section 10.1.2, for use by other researchers including those outside of the study. Permission to transmit data to these data repositories will be included in the informed consent, in section 10.1.2.

10.1.4 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	Medical Monitor
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<i>Louise Laurent, MD PhD, Professor and Vice Chair for Translational Research and Director of Perinatal Research</i>	<i>N/A</i>
<i>UC San Diego</i>	<i>Institution Name</i>
<i>9500 Gilman Drive MC 0695, La Jolla, CA 92093</i>	<i>Address</i>
<i>858-336- 6882</i>	<i>Phone Number</i>
<i>Llaurent@health.ucsd.edu</i>	<i>Email</i>

Not Applicable

10.1.5 SAFETY OVERSIGHT

An Independent Data Monitoring Committee (IDMC) will be formed and used to monitor safety compliance and data collection during the duration of the study. The IDMC activities and goals are developed based on the National Institute of Environmental and Health Sciences (NIEHS) guidelines.

I. Type of Monitoring

Routine Monitoring will be used during the study. Routine monitoring will be based on the National Institute of Environmental and Health Sciences (NIEHS) standard definition of study monitoring types.

II. Independent Data Monitoring Committee (IDMC) Membership

1. Total IDMC members

- There will be 6 Total members, all of which will be Voting members, with a quorum of 4 for each meeting. Any decisions made must have the agreement of the Chair.

2. Chair of the IDMC

- Selected by the voting members prior to the start of the study
- Term duration will be one academic year and renewable for two terms

3. Voting members include at least one member from each of the following groups: Infectious Disease physician, Epidemiologist, Community Engagement Researcher, Bioethicist/Legal expert, and Patient Advocate (from CSAB).

III. Independent Data Monitoring Committee (IDMC) Responsibilities (obtained from NIEHS guidelines: <https://www.niehs.nih.gov/research/clinical/patientprotections/dsmb/index.cfm>)

1. Prior to study initiation the following will be reviewed by the IDMC committee

- Research protocol and informed consent forms
- Safety monitoring protocol and protocol to report adverse events.
- Methods of maintaining confidentiality

2. Throughout the study the following will be reviewed

- Compliance with safety protocols
- Any deviations from research protocol
- Periodic review of signed informed consent forms.

- d. Participant recruitment, accrual and retention, participant risk versus benefit
- e. Return of results and effects on clinical management
- f. Review of external literature as the study proceeds forward to identify any relevant new studies that show scientific evidence of therapeutic benefits or newly demonstrated adverse effects of WGS for prenatal or postnatal diagnosis of fetal anomalies, IUGR, and/or stillbirth.
- g. Review of any perceived problems with study conduct, enrollment, sample size, and/or data collection
- 3. Have the power to give recommendations regarding continuation, termination or other modifications of the study-based review of ongoing events
- IV. Frequency, Records, and Summaries of IDMC Meetings:
 - Frequency: Every 6 months with Ad hoc meetings as needed.
 - Type of session: Open sessions
 - Documentation: All meetings will have a summary of record that the meeting, stating date, time and type of meeting (telephone, in person, video conference call); a list of participants.
- V. List of Adverse Events

Scope of Adverse Events: The list below provides information of potential events that may be encountered and steps that the investigators have taken to manage them.

- 1. Loss of confidentiality (Significant Adverse Event). All PHI will be stored in password-protected documents on password-protected computers kept in locked rooms.
- VI. Reporting Requirements for Adverse Events

All adverse events will be reported to the IRB and IDMC within 24 hours.

10.1.6 CLINICAL MONITORING

A clinical monitoring plan is not required for this project.

10.1.7 DATA HANDLING AND RECORD KEEPING

10.1.7.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical research staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. All consent documents and survey data for each participant enrolled in the study will be stored in REDCap. Research data collected will be coded with a participant's unique identifier, or number. Personal identifying data will not appear on any research data.

All computer screens will have a five-minute time limit that will produce a blank screen if left unattended and will require a password to re-access the screen. This database will only be available to the project team.

All individuals working on the study will sign confidentiality agreements to never disclose any individual information regarding any aspect of the study. As it true for all UCSD personnel, any person(s) working on this research project will have undergone extensive orientation and training on issues regarding the maintenance and protection of confidentiality (e.g., sending confidential material to a community printer, using names while conducting phone interviews, etc.).

10.1.7.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 3 years after the last approval of a marketing application in an International Conference on Harmonisation (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 3 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

45 Code of Regulations (CFR) part74.53 requires awardees to retain records pertinent to an award for a period of three years from the date of submission of the final expenditure report or, for awards that are renewed quarterly or annually, from the date of the submission of the quarterly or annual financial report.

10.1.8 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, section 5.1.1
- 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation. All deviations must be addressed in study source documents, reported to the NIH Program Official and Duke Clinical Research Institute. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.2 ADDITIONAL CONSIDERATIONS

Translation Services

All documents will be translated from English to Spanish by the RADx-UP program with Duke Clinical Research Institute.

A second review of translations are completed by San Ysidro Health Centers research staff. Translation attestations will be uploaded in supporting information.

CSAB Information Sheet Consent

Cohort 1 is comprised of the CSAB members who will be focusing on the refinement and evaluation of the COVID-19 testing strategies. Each of their meetings will be conducted virtually. We are requesting a waiver of documented consent and we are asking to use the information sheet to obtain verbal consent of each CSAB member. The verbal informational sheet consent was used successfully in our currently funded RADx-UP CO-CREATE 1.0 project for our CSAB members. We judge verbal consent is sufficient because their participation in this research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

Interview Guides & Consent

Interview guides for both participants in Cohort 2 and providers/staff in Cohort 3 will be developed after pre-mortem brainwriting exercises with CSAB members. These guides will be submitted to the IRB after they are developed for approval. Similarly, to the CSAB information sheet consent, we are requesting a waiver of documented consent to conduct these interviews. We plan to use the information sheet to obtain verbal consent as each of these interviews will be conducted virtually. We judge verbal consent is sufficient because their participant in this research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

10.3 ABBREVIATIONS

AE	Adverse Event
ACTRI	Altman Clinical and Translational Research Institute
ANCOVA	Analysis of Covariance
ARC	Global Action Research Center
CDEs	Common data elements
CDCC	Coordination and Data Collection Center
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CO-CREATE-EX	<u>C</u> ommunity-engaged <u>O</u> ptimization of <u>C</u> OVID-19 <u>R</u> apid <u>E</u> valuation <u>A</u> nd <u>T</u> esting <u>E</u> xperiences
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CSAB	Community and Scientific Advisory Board
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FFR	Federal Financial Report
GCP	Good Clinical Practice
Global ARC	Global Action Research Center
GMP	Good Manufacturing Practices
HIPAA	Health Insurance Portability and Accountability Act
IDMC	Independent Data Monitoring Committee
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
MPI	Multi-Principal Investigator
NCT	National Clinical Trial
NIH	National Institutes of Health
NIEHS	National Institute of Environmental and Health Sciences

OHRP	Office for Human Research Protections
PI	Principal Investigator
PRISM	Practical, Robust Implementations and Sustainability Model
QA	Quality Assurance
QC	Quality Control
RADx-Up	Rapid Acceleration of Diagnostics in Underserved Populations
RAT	Rapid antigen test
ROIO	Roll-out implementation optimization
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOP	Standard Operating Procedure
SYH	San Ysidro Health
UP	Unanticipated Problem
US	United States

[illegible]

11 REFERENCES

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