Rapid Acceleration for Diagnostics in Underserved Populations: HOme Testing (RADx-UP HoT)

National Clinical Trial (NCT) Identified Number: Pending

Principal Investigators: Christoph Hornik, MD PhD MPH

Co-Investigators: Giselle Corbie-Smith, MD, MSc

Gaurav Dave, MD, DrPH, MPH

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Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
Sections 1.1, 1.3, 4.1, 4.4, and 9.3	The at-home testing through the public health intervention will be 3 times a week for 4 weeks, instead of testing twice a week for 5 weeks.	More frequent testing is better suited to diagnosing asymptomatic/pre-symptomatic disease and prevent spread.
Section 1.3	Questionnaires/surveys will be administered only on baseline and weeks 1, 3, 5, 13, and 21. The Schedule of Events table has been updated to reflect these timepoints.	To reduce participant burden, questionnaires/surveys will only be administered on baseline and weeks, 1, 3, 5, 13, 21.
Section 1.3	The survey on knowledge of prevention approaches will be administered on weeks 5 and 21 instead of weeks 13 and 21.	Administering this questionnaire at week 5 and week 21 allows for a better perceptive to see how the participant's knowledge has changed over time.
Section 1.3	The survey on feasibility of at-home testing has been removed from week 21. It will only be administered at week 5.	To reduce participant burden, this survey will only be asked once after the testing phase.
Section 1.3	Survey questions on Beliefs were added to the protocol for weeks 1, 5, and 21.	No new questions were added. The survey questions on Belief were already included in the questionnaire. It has now been specified as a new category of questions within the protocol.
Section 1.3	Anthropometrics (weight) was added as a measure to be taken at Baseline and week 5. Anthropometrics (height) was added as a measure to be taken at Baseline.	Socio-Demographic Data was already planned at Screening and Enrollment (now called Baseline). For additional clarity, anthropometrics have now been specified at Baseline. Height will be taken at Baseline. Since weight fluctuates, it will be taken at Baseline and week 5.

Section 1.3	Contact information will be collected during the Screening and Enrollment phase. It has been added to Schedule of Events table under Baseline.	Contact information was already planned to be collected. For additional clarity, it has now been added to the Schedule of Events table.
Sections 3 and 9.4.4	The method used for the exploratory objective to measure participant mobility was changed from mobile phone geotracking to surrogates of mobility including activity tracker.	The method of mobility tracking was updated since the smartphone application for this study is expected to be able to access activity tracking functions of the phones on which the application is installed.

STUDY PRINCIPAL INVESTIGATORS

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable federal regulations and ICH guidelines.

Principal Investigator Signature

Christoph Hornik

Electronically signed by: Christoph Hornik
Reason: Approved
Date: May 20, 2021 17:09 EDT

Christoph P. Hornik, MD PhD MPH — Date

Co-Investigators Signatures

Electronically signed by: Giselle Corbie-Smith
Reason: Approved
Date: May 24, 2021 12:23 EDT

Giselle Corbie-Smith, MD, MSc — Date

Electronically signed by: Gaurav Dave
Reason: Approved
Date: May 20, 2021 21:40 EDT

Gaurav Dave, MD, DrPH, MPH — Date

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STATEMENT OF COMPLIANCE

The study will be carried out in accordance with International Conference on Harmonization Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812)

National Institutes of Health (NIH)-funded investigators and study staff who are responsible for the conduct, management, or oversight of NIH-funded studies have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: Rapid Acceleration for Diagnostics in Underserved Populations: Home Testing (RADx-UP HoT)

Study Description: This observational, cohort sub-study is embedded within a larger public health intervention that distributes at-home, self-administered, SARS-CoV-2 antigen testing kits to households within pre-selected communities through the CDC. Within this sub-study, we will evaluate the socio-behavioral mechanisms of SARS-CoV-2 community transmission, including social interactions, health behaviors, healthcare utilization, knowledge, disease burden, and feasibility of at-home testing. The study hypothesis is that positive at-home test results will be associated with altered self-reported social interactions and altered health behaviors compared to negative test results. Surveys and questionnaires will be completed by participants through the smartphone app or via call center phone calls according to the schedule of events. Questionnaires will collect data on demographic characteristics, medical history and health status, COVID testing and symptoms, social interactions, knowledge of prevention strategies, infection risk, and attitudes towards vaccines.

Objectives: Primary Objective:

- To assess self-reported social interactions following SARS CoV-2 at-home test result over the study period

Secondary Objectives:

- To assess change in self-reported behaviors before and following SARS CoV-2 at-home test result over the study period
- To assess the impact of at-home testing regimen on self-reported healthcare utilization for SARS CoV-2 treatment
- To assess knowledge of SARS CoV-2 prevention approaches over the study period

Endpoints: Primary Endpoint:

- Proportion of respondents that report adhering to social distancing guidelines after a test result; comparison of proportion adherent after positive vs. negative test result

Secondary Endpoints:

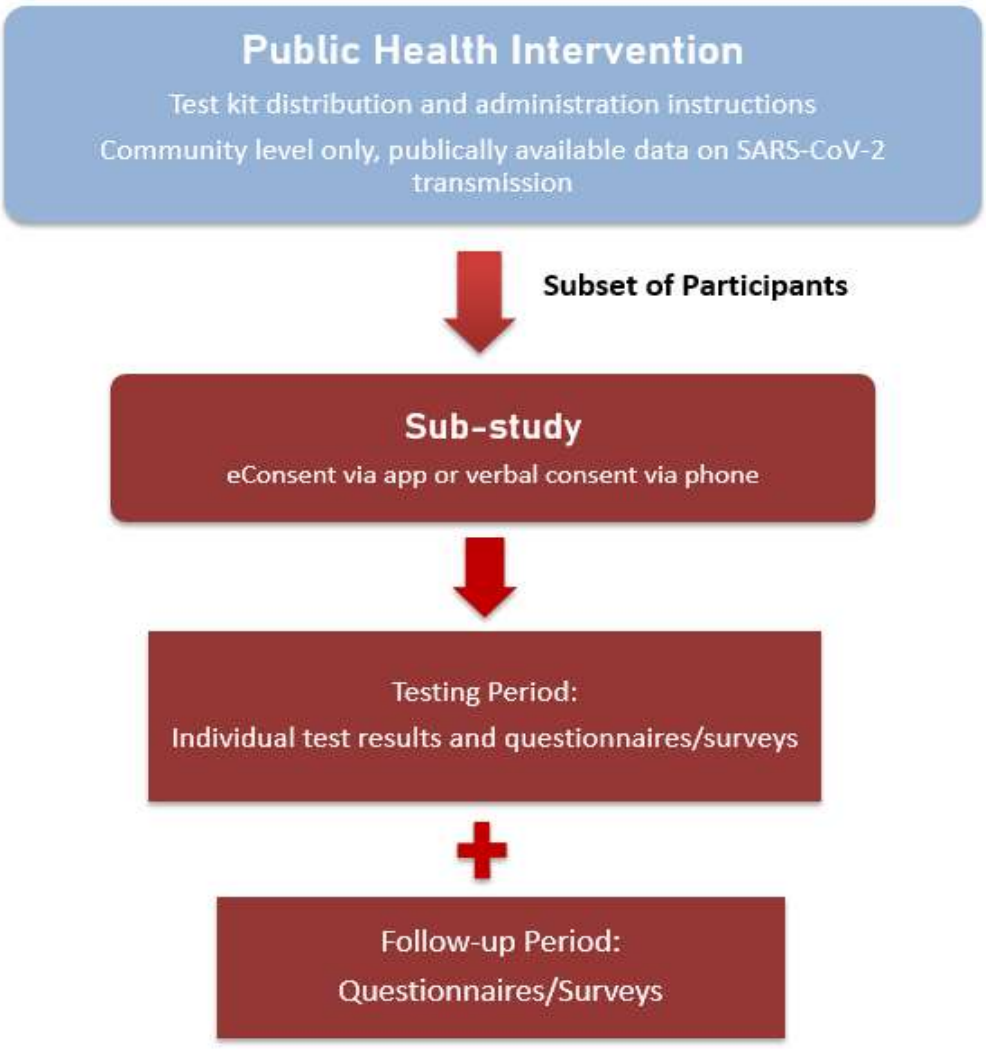
- Proportion of respondents that decide to act on precautionary behaviors after a test result
- Point estimate and 95% confidence interval for each healthcare utilization measure and composite measure
- Proportion of respondents that are knowledgeable of precautionary measures to prevent infection
- Prevalence of positive test results with 95% confidence intervals

Study Population: Adults and children > 8 years of age living within pre-identified communities participating in the public health intervention

Phase: Not applicable

Description of Sites/Facilities Enrolling Participants:	This is a site-less, direct to participant study. Participants, up to 300,000, will be recruited for the sub-study within the communities participating in the larger public health intervention.
Description of Study Intervention:	Collection of survey data
Study Duration:	Total of up to 29 weeks, including up to 4 weeks of screening period and 25 weeks from the start of the study.
Participant Duration:	Up to 25 weeks: 4 weeks of active testing period and 17 weeks of follow-up. Last follow-up will be at week 21 with a 4 week window (up to week 25) to complete the surveys.

1.2 SCHEMA



1.3 SCHEDULE OF ACTIVITIES (SOA)

Study Period/Phase:	Screening & Enrollment Phase		Sub-study Questionnaires/Surveys							Comments & Notes
			Testing Phase (Public Health Intervention)*				Follow-Up Phase			
Week:	Weeks– 4 to 0	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5	Week 13	Week 21	
Informed Consent and Assent when applicable		X								e-Consent via app or verbal consent via call center
Create mobile app account		X								For participants using the mobile app
Contact Information		X								
Socio-Demographic Data		X								
Medical History		X								
Anthropometrics – Weight		X					X			
Anthropometrics – Height		X								
Questionnaires										Questionnaires can be completed during the week after each test (regardless of the result).
• **Social interactions** • **Behaviors** • **Symptoms** • **Healthcare utilization**		X	X		X		X	X	X	
• **Beliefs**		X	X				X		X	
• **Knowledge of prevention approaches**							X		X	
• **Feasibility of at-home testing**							X			
Testing Adherence/Compliance reminders			X	X	X	X	X	X	X	

*The public health intervention (3 times a week at-home testing) does not require consent. Consent is only required for this sub-study which involves the questionnaires/surveys that are administered during the testing phase and follow-up phase.

2 INTRODUCTION

2.1 STUDY RATIONALE

The public health crisis of the COVID-19 pandemic continues to rage on across the US. Novel mitigation strategies and community level public health interventions are critical to stop the spread of this virus. One of these interventions is frequent, low-cost, rapid-result, at-home viral screening of asymptomatic and symptomatic individuals. The goal of frequent home testing is to identify SARS-CoV-2 index cases early, trigger isolation and quarantining precautions, and ultimately decrease community transmission.

The Centers for Disease Control, through coordination with public health departments, is conducting a public health intervention of frequent home testing, completed in a timeline needed to address the pressing need in high-risk communities. This intervention of home testing requires intentional engagement and a clear recognition of risk. Within pre-selected communities, CDC will distribute at-home, self-collect/self-test SARS-CoV-2 tests with instructions to complete regular testing irrespective of symptoms or exposure history. Previous at-home testing studies have generated inconclusive results, in part due to multiple factors including inadequate community engagement strategies to promote uptake and consistent testing in the target population as well as limited testing and prevention knowledge, attitudes and behavior.

This cohort sub-study in a subset of the population will explore the community and human behavior factors in response to at-home testing. Participants in the public health intervention who meet eligibility criteria will be invited to participate in the sub-study, consented, and asked to complete questionnaires aimed at evaluating self-reported social interactions, behaviors, and health system utilization in response to results from the at-home SARS CoV-2 antigen test. This sub-study will provide participant level behavioral information essential to understanding the relationship between large scale at-home testing and community transmission during the SARS-CoV-2 pandemic and relevant for implementation of public health interventions in future pandemics.

2.2 BACKGROUND

In the US, > 4 million people have been infected with the SARS-CoV-2 virus and >400,000 died. Infections and deaths, however, have disproportionally affected historically marginalized populations. Early in the pandemic the focus has been on testing to identify symptomatic individuals to reduce morbidity and mortality from infection. As public health measures have scaled up mitigation strategies are increasingly being considered to reduce community spread of infection. The availability of rapid tests for detecting SARS-CoV-2 presents opportunities for rapid, frequent and low-cost at-home testing in asymptomatic populations as part of a broader mitigation strategy that includes protective measures (masking, social distancing, increased hygiene) and contact-tracing and isolation. With 50% or more of infections resulting from pre-symptomatic or asymptomatic transmission, at-home testing may offer an effective option for screening and for breaking chains of transmission. Rapid antigen tests are relatively inexpensive and therefore can be used frequently for detecting infected individuals who are asymptomatic, pre-symptomatic and without known or suspected exposure to SARS-CoV-2[1]. However, even with antigen tests, the implementation of community level testing will be challenging, with an impact that is still to be determined[2].

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Study-related risks include potential loss of confidentiality but steps will be undertaken to minimize this risk. There are no interventions involved in this study.

2.3.2 KNOWN POTENTIAL BENEFITS

The benefit of this study is to learn testing impact on reducing the community spread of the infection, however there is no direct benefit to participants.

3 OBJECTIVES AND ENDPOINTS

Objectives	Outcome Measures	Endpoint
Primary		
1. To assess self-reported social interactions following SARS CoV-2 at-home test result over the study period	Assessments: self-reported data on social distancing, quarantine, social connectedness, healthcare utilization, well-being	Proportion of respondents that report adhering to social distancing guidelines after a test result for the entire study cohort and stratified by participant demographics (e.g., sex) of interest; comparison of proportion adherent after positive vs. negative test result
Secondary		
2. To assess change in self-reported behaviors before and following SARS CoV-2 at-home test result over the study period	Assessments: self-reported data on awareness of the issue, engagement, decisions to act, action, and maintenance	Proportion of respondents that decide to act on precautionary behaviors after a test result for the entire study cohort and stratified by participant demographics (e.g., gender) of interest
3. To assess the impact of at-home testing regimen on self-reported healthcare utilization for SARS CoV-2 treatment	Assessments: self-reported ED visits, hospitalizations, and ICU admission, for SARS CoV-2 evaluation or treatment	Point estimate and 95% confidence interval for each healthcare utilization measure and composite measure for the entire study cohort and stratified by participant demographics (e.g., gender) of interest
4. To assess knowledge of SARS CoV-2 prevention approaches over the study period	Assessments: self-reported data on perceptions and prevention of risks of contracting SARS CoV-2 infection	Proportion of respondents that are knowledgeable of precautionary measures to prevent infection for the entire study cohort and stratified by participant demographics (e.g., gender) of interest
5. Prevalence of positive test result for SARS CoV-2	Assessments: reported results of self-administered SARS CoV-2 antigen test	Prevalence of positive test results with 95% confidence intervals for the entire study cohort and stratified by participant demographic variables of interest

Exploratory		
6. To assess the feasibility of at-home self-administered SARS CoV-2 antigen tests	Assessments: self-reported data on acceptability, practicality, integration, penetration, and demand of at-home self-administered antigen test	Proportion of respondents that find at-home self-administered antigen test acceptable for the entire study cohort and stratified by participant demographics (e.g., gender) of interest
7. To assess participant mobility following SARS CoV-2 at-home test results over the study period	Assessment: mobility patterns as captured by surrogates including activity trackers	Distribution of individual mobility data in response to positive vs. Negative SARS CoV-2 test results.
8. To assess attitudes towards SARS CoV-2 vaccination over the study period	Assessments: self-reported data on perceived susceptibility, severity, benefits, barriers, and cues to action related to SARS CoV-2 vaccination	Distribution of respondent's perception about SARS CoV-2 vaccination for the entire study cohort and stratified by participant demographics (e.g., gender) of interest

4 STUDY DESIGN

4.1 OVERALL DESIGN

This is an observational, direct-to-participant, nested cohort, sub-study embedded within a public health intervention that distributes at-home, self-administered, SARS-CoV-2 antigen testing kits. Adults and children over 8 years of age living within the pre-identified communities will be included. This sub-study focuses on gathering participant-level data to evaluate behavioral determinants of home testing and socio-behavioral mechanisms of SARS-CoV-2 community transmission.

The smartphone application developed by CareEvolution, called MyDataHelps, will be used for this study, and it is free of charge on Apple or Android devices[3]. As part of the public health intervention, households will receive test kits and included in them will be information about the app and a QR code to facilitate access. Only after the participants have received information about the public health intervention and received the testing kits, will they be offered the option to participate in this sub-study. Once registered, if the participant wants to be a part of the sub-study, eligibility criteria will be verified and e-consent will be obtained through the app. The smartphone app includes instructions to administer at-home tests, for all participants in the public health intervention. Push notifications will be programmed with messaging to promote adherence including personalization, context, and timing for all pariticipants in the public health intervention. Additionally, participants will have an option to opt-in to reminders for testing 3 times a week at a time of their preference. For participants who provide consent to the sub-study, the app will also feature the ability to report the results of their test results (upload images of test trips), track testing history, respond to surveys and questionnaires, and access study team's contact information. As an alternative to the app, participants can participate in the study via phone interviews conducted by a centralized study call center. Home test kits will include a QR code for the public health intervention app which will link to DCRI call center/eConsent for those interested in participating. Using scripted interview guides, call center staff will be ready to explain study participation, obtain verbal consent, administer study questionnaires including soliciting test results, and issue phone reminders for participants who chose not to use the study app.

Using PhenX and Common Data Element (CDE) measures, the surveys and questionnaires will collect data on demographic characteristics, medical history and health status, SARS-CoV-2 testing and symptoms, social interactions, knowledge of prevention strategies, and infection risk, and attitudes towards vaccines.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

This study involves a direct-to-participant approach that minimizes participant burden and accelerates translation of study findings into daily life settings. This study designs bypasses the traditional settings within healthcare environments, and instead brings study procedures to the participants' homes. A direct-to-participant approach minimizes risks by leveraging the public health intervention community engagement, recruitment, and intervention dissemination efforts, and maximizes rewards by selectively complementing study data with participant specific information on behaviors and clinical outcomes associated with frequent at-home testing.

The objective of the study is to gather participant level information about social behaviors in response to at-home test results during the SARS-CoV-2 pandemic. Therefore, a direct-to-participant design, which maximally integrates assessments into participant's lifestyle was deemed best suited to provide accurate representation of behaviors.

There are certain limitations to this study design. A slow enrollment is the greatest challenge to any prospective cohort study. By nesting the sub-study within the public health intervention, the sub-study leverages the multimodal community engagement and kit dissemination strategies of the public health intervention. Non-compliance with study procedures is a risk for community based and direct-to-participant studies, where traditional health care visits are not available to perform procedures or reinforce compliance. Participation will be facilitated by creating two participation pathways, app and call center enabled.

As a result of these efforts, the goal is to establish a systematic approach combining community engagement and at-home testing to decrease transmission of SARS-CoV-2 as well as inform public health interventions for future pandemics.

4.3 JUSTIFICATION FOR DOSE

There is no study specified administration of a test product. The SARS-CoV-2 test is being self-administered as part of the public health intervention, and is not part of this sub-study protocol.

4.4 END OF STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed the active testing period (at-home testing 3 times a week for 4 weeks) along with the questionnaires/surveys during those 4 weeks. Questionnaires/surveys will continue to be offered during the follow-up period (up to 17 weeks). Any amount of testing data and survey responses completed will be acceptable and analyzed.

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:

1. Self-reported primary residence within the pre-identified communities
2. Age > 8 years at enrollment
3. Provision of signed and dated informed consent form

5.2 EXCLUSION CRITERIA

There are no exclusion criteria for this study, if all above inclusion criteria are met.

5.3 LIFESTYLE CONSIDERATIONS

Not applicable

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in the sub-study but are not subsequently entered in the study because they do not meet the inclusion criteria for participation or decide not to participate at anytime

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Participants for this sub-study will be recruited within the communities participating in the larger public health intervention. Recruitment strategies include marketing with public health messaging in collaboration with local health departments, media and targeted social media outreach for awareness and education, as well as other strategies that would be tailored to the different distribution scenarios. Participants may be compensated up to $50 for completion of all surveys. The sample size is up to 300,000 for the sub-study. The test kits distributed as part of the larger study will contain information about the sub-study and how-to consent using either a mobile device based application (e-consent) accessible free of charge to participants or via phone consenting (verbal consent). All participants who consent to the sub-study could be re-contacted for future research opportunities. An option to opt-out of re-contacting will be provided in the consent.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

The smartphone app used in this study, MyDataHelps, is an NIH funded app that uses secure file transfer protocols and can administer consent forms, surveys, and capture multimedia information.

6.1.2 DOSING AND ADMINISTRATION

Not Applicable

6.2 PREPARATION/HANDLING/STORAGE/ACCOUNTABILITY

Not Applicable

6.2.1 ACQUISITION AND ACCOUNTABILITY

Not Applicable

6.2.2 FORMULATION, APPEARANCE, PACKAGING, AND LABELING NOT APPLICABLE

Not Applicable

6.2.3 PRODUCT STORAGE AND STABILITY

Not Applicable

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

This study will be conducted as a non-randomized cohort sub-study design to assess the individual social behavior during a community level at-home testing program. Eligible communities receiving will be selected per criteria in the public health intervention.

6.4 STUDY INTERVENTION COMPLIANCE

Push notifications will be programmed in the app along with text messaging to promote adherence to the at-home testing schedule as well as the survey and questionnaire schedule as part of the public health intervention The app also includes a personal tracker of participant test history. Phone call reminders will be provided for participants who choose not to use the app. Deviations to the public health intervention will not be tracked.

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

No study intervention-not applicable

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time. The reason for participant discontinuation or withdrawal from the study will be collected on the app or through phone call via call center. Participants who provide consent, and subsequently withdraw, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to complete the at-home testing and scheduled questionnaires/surveys and is unable to be contacted by the call center.

The DCRI call center will attempt to contact the participant and counsel the participant on the importance of maintaining the assigned study schedule and ascertain if the participant wishes to and/or should continue in the study. Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 EFFICACY ASSESSMENTS

The questionnaires/surveys will assess patient-report outcomes related to social behaviors, healthcare utilization, knowledge of SARS CoV-2 prevention approaches, and the feasibility of at-home self-administered testing. Adherence to the at-home testing and questionnaire/survey schedule will also be assessed.

8.2 SAFETY AND OTHER ASSESSMENTS

The healthcare utilization questionnaire will be routinely administered during the treatment and follow-up phase, and it will ask about any emergency department visits, hospitalizations, and ICU admission related to SARS COV-2 evaluation or treatment.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

Not applicable

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

Not applicable

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

Not applicable

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

Not applicable

8.3.5 ADVERSE EVENT AND SERIOUS ADVERSE EVENT REPORTING

Not applicable

9 STATISTICAL CONSIDERATIONS

Additional details of the planned statistical analyses will be provided in a separate statistical analysis plan.

9.1 STATISTICAL HYPOTHESES

The proposed analysis is primarily descriptive rather than inferential, as it designed to provide a general assessment of participant level behaviors in the context of a community testing intervention. An exploratory hypothesize is that positive at-home SARS-CoV-2 antigen test results will lead to altered self-reported social interactions and altered health behaviors compared to negative test results.

9.2 SAMPLE SIZE DETERMINATION

A formal power calculation is not performed for this observational cohort study. However, a sample size in the ranges of 1000 to 10,000 participants would be sufficient to estimate positive test incidence and prevalence, describe behavioral changes associated with test results, and conduct multivariable modeling to inform understanding of the causal chain between frequent testing and community burden of disease. To illustrate this, suppose the proportion of participants who adhere to social distancing is 50%. In that case, a sample size of 5,000 participants will be sufficient at a confidence level of 95% to estimate the prevalence with a margin of error of 1.5%. Additional examples of estimate precision at varying sample sizes are provided below. Overall, even with a sample size of 1000 participants and for an endpoint with a 50% proportion, there will be a 95% chance that the real value of this proportion is within 3.1% of the observed value.

Sample Size N=	Point estimate of proportion	Margin of error
10,000	1%	0.19%
10,000	10%	0.58%
10,000	50%	0.96%
10,000	80%	0.77%
5000	1%	0.27%
5000	10%	0.82%
5000	50%	1.37%
5000	80%	1.10%
1000	1%	0.62%
1000	10%	1.86%
1000	50%	3.09%
1000	80%	2.48%

9.3 POPULATIONS FOR ANALYSES

The following populations are also defined:

Population	**Description**
Evaluable Population- Per protocol (PP)	Per protocol population will be those that report adhering to the following: 1. Self-administer the at-home test three times a week for 4 weeks 2. Complete questionnaires/surveys during the 4 week testing period
Modified per-protocol	Will include any participant who performed at least one at-home test
Second modified per-protocol	Will include any participant who completed at least one survey

All analyses will be conducted in the PP. A subset of analyses will be repeated in the modified PP populations as applicable.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

The approach to analysis will be primarily descriptive. Demographics, questionnaire data, and testing results will be reviewed and summarized using graphical techniques and summary statistics. Where applicable, exact method confidence intervals will be computed around point estimates. Trends over time will be evaluated graphically. The proportion of participants adhering to social distancing guidelines after a positive vs. negative test result will be compared using tests of proportion clustered by participants with various levels of intra-participant correlation. Stratified analyses by test or week number will also be performed. We will explore the associations between positive test results and critical behavioral measures using mixed modeling techniques to account for the participant and

household correlations. Analyses will be conducted using SAS (SAS Institute, Cary NC) and R with R Studio (R-project).

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

Point estimates with 95% confidence intervals will be reported. The analysis will be done for applicable study populations as described above, and stratified by participant demographics of interest (e.g., age, gender). There will be a comparison of the proportion of participants that report adhering to social distancing guidelines after positive vs. negative test result.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

- The first secondary objective is to assess change in self-reported behaviors before and following SARS CoV-2 at-home test result over the study period. This will be measured via Precaution Adoption Process Model Assessments of self-reported data on awareness of the issue, engagement, decisions to act, action, and maintenance. The proportion of respondents that decide to act on precautionary behaviors after a test result will be analyzed for the entire study cohort and stratified by participant demographics of interest (e.g., age, gender).

- The second secondary objective is to assess the impact of at-home testing regimen on self-reported healthcare utilization for SARS CoV-2 treatment. This will be measured via self-reported Emergency Department visits, hospitalizations, and ICU admission for SARS CoV-2 evaluation or treatment. The proportion of respondents that decide to act on precautionary behaviors after a test result will be analyzed for the entire study cohort and stratified by participant demographics of interest (e.g., age, gender).
- The third secondary objective is to assess knowledge of SARS CoV-2 prevention approaches over the study period. This will be measured via self-reported data on perceptions and prevention of risks of contracting SARS CoV-2 infection. The proportion of respondents that are knowledgeable of precautionary measures to prevent infection will be analyzed for the entire study cohort and stratified by participant demographics of interest (e.g., age, gender).

- The fourth secondary objective is to assess prevalence of positive test result for SARS CoV-2. This will be measured via self-reported results of self-administered SARS CoV-2 antigen test. The prevalence of positive test results will be analyzed with 95% confidence for the entire study cohort and stratified by participant demographics of interest (e.g., age, gender).

9.4.4 ANALYSIS OF THE EXPLORATORY ENDPOINTS

- The first exploratory objective is to assess the feasibility of at-home self-administered SARS CoV-2 antigen tests. This will be measured via self-reported data on acceptability, practicality, integration, penetration, and demand of at-home self-administered antigen test. The proportion of respondents that find at-home self-administered antigen test acceptable will be analyzed for the entire study cohort and stratified by participant demographics (e.g., age, gender).

- The second exploratory objective is to assess participant mobility following SARS CoV-2 at-home test results over the study period. This will be evaluated using surrogate of mobility, including activity trackers.

- The third exploratory objective is to assess attitudes towards SARS CoV-2 vaccination over the study period. This will be measured via Health Belief Model Assessments using self-reported data on perceived susceptibility, severity, benefits, barriers, and cues to action related to SARS CoV-2 vaccination. The distribution of respondent's perception about SARS CoV-2 vaccination will be analyzed for the entire study cohort and stratified by participant demographics (e.g., age, gender).

9.4.5 SAFETY ANALYSES

Not Applicable

9.4.6 BASELINE DESCRIPTIVE STATISTICS

Will be reported for demographic and medical history information.

9.4.7 PLANNED INTERIM ANALYSES

Not Applicable

9.4.8 SUB-GROUP ANALYSES

The majority of the primary, secondary, and exploratory endpoints analyses will also be stratified based on age, sex, race/ethnicity or other demographic characteristics.

9.4.9 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data and listings may be analyzed as needed during the study.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail study procedures, and risks are given to the participants via the app (eConsent) or read to the participants through the phone (verbal consent). Informed consent is required prior to enrollment in this study. The following consent materials are submitted with this protocol: Adult ICF (above age 18), Age of Majority ICF (for those who turn 18 during the course of the study), and the Assent (below age 18).

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved. Individuals participating via the app will be asked to read, review and electronically give their consent directly on the app. For individuals participating via the phone, the call center staff will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to ask questions prior to giving their verbal consent. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. The informed consent process will be conducted and documented, including the date consented, before the participant undergoes any study-specific procedures.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, funding agency, the sponsor and regulatory authorities. If the study is prematurely terminated or suspended, PI will promptly inform study participants, the 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 to study schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements

- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor and IRB.

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor and their interventions. No information concerning the study or the individual participant data will be released to any unauthorized third party without prior written approval of the sponsor.

The study participant's contact information will be securely saved for internal use during the study. At the end of the study, all records will continue to be saved securely for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data collected via the app or the call center, which is for purposes of statistical analysis and scientific reporting, will be securely stored. This will not include the participant's contact or identifying information. Data transmitted to CareEvolution will be de-identified when extracted by the study team. Information collected by the CareEvolution app will be securely stored on CareEvolution servers in the United States, or on servers owned by third party service providers that CareEvolution contracts with to securely store information in the United States. The study data entry and study management systems will be secured and password protected. At the end of the study, all study data from the app will be de-identified and archived.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data generated from this study will be analyzed in this study. In addition, the NIH Data Sharing Policy applies to this study, and de-identified data from this study will be made available to other researchers.

No data will be shared with the test manufacturer and the data generated in this study will not be used to support any regulatory claims.

All participants in the sub-study will have the option to consent to re-contacting for future research. An option to opt-out of re-contacting will also be provided in the consent.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	Co-Investigator	Co-Investigator
Christoph Hornik, MD, PhD, MPH	Giselle Corbie-Smith, MD, MSc	Gaurav Dave, MD, DrPH, MPH
Duke Clinical Research Institute	University of North Carolina	University of North Carolina
300 W. Morgan Street Durham, NC 27701	333 South Columbia Street Chapel Hill NC 27599-7240	160 N Medical Rd, Chapel Hill, NC 27599.
919-668-8935	919-962-1136	919-843-9632
christoph.hornik@duke.edu	gcorbie@med.unc.edu	gjdave@unc.edu

10.1.6 SAFETY OVERSIGHT

Since there are no medications or interventions being prescribed as part of the study, and due to the minimal risk of the survey data only the study will not have a Data and Safety Monitoring Board (DSMB). Instead, the DCRI PI will serve as the medical monitor.

10.1.7 CLINICAL MONITORING

As a direct-to-family study, the study will take place directly in a participant's home and there will be no formal monitoring of the study. Study personnel will still ensure that the rights and well-being of study participants are protected, that the reported study data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the currently approved protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

The DCRI will perform internal quality management of study conduct, data collection, documentation and completion.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database. The study team will be responsible for monitoring data collected via the mobile application to ensure that the reported study data are accurate, and complete, reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The study team will provide access to all study related source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Using PhenX and RADx-Up CDE measures, the questionnaires/surveys will collect data on demographic characteristics, medical history and health status, SARS-CoV-2 testing and symptoms, social interactions, knowledge of prevention strategies, and infection risk, and attitudes towards vaccines. All data capture will be electronic for participants who choose to participate using the MyDataHelps app. The app platform will be the technology that underpins data collection and management. The mobile application functions as a communication platform between the participants, investigators, and the study team. It supports daily reminders, seamless data collection, surveys/questionnaires, and data exchange between participants and the study team. In addition to its function as a communication platform, it is also a source documentation platform that is used to record, document, and store all information collected by the study team. All source data entered into the application has an audit trail, which documents who completes data entry and when, with all data legibly recorded. Study team members entering source data into the application do so in real time as they are collecting the data. For those participating via the phone calls, the data provided by the participant will be documented into the app by the call center member.

10.1.9.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 2 years after the last approval of a marketing application in an International Conference on Harmonization (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 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.

10.1.10 PROTOCOL DEVIATIONS

Protocol deviations will not be collected or tracked for this observational study.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this study will be registered at ClinicalTrials.gov, and results information from this study will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 10 years after the completion of the primary endpoint by contacting Dr. Christoph Hornik or Dr. Gaurav Dave.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this study will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this study. The study leadership in conjunction with the NIH Institute has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ABBREVIATIONS

AE	Adverse Event
CFR	Code of Federal Regulations
CRF	Case Report Form
DCC	Data Coordinating Center
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
SOE	Nares swab
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
RADX-UP	Rapid Acceleration for Diagnostics in Underserved Populations
SAE	Serious Adverse Event
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
US	United States

10.3 PROTOCOL AMENDMENT HISTORY

The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A Summary of Changes table for the current amendment is located in the Protocol Title Page.

Version	Date	Description of Change	Brief Rationale

11 REFERENCES

1. Toptan T, Eckermann L, Pfeiffer AE, et al. Evaluation of a SARS-CoV-2 rapid antigen test: Potential to help reduce community spread? *J Clin Virol.* 2020;135:104713.
2. Bosetti P, Kiem CT, Yazdanpanah Y, et al. Impact of mass testing during an epidemic rebound of SARS-CoV-2: a modelling study using the example of France. *Euro Surveill.* 2021;26(1).
3. CareEvolution L CareEvolution, LLC. *https://careevolution.com/*. Accessed January 17, 2021.

RADx-HoT Protocol v2.0 Signature

Final Audit Report 2021-05-24

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By:	Saranya Venkatachalam (sv209@duke.edu)
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