Identifying Optimal Testing Modalities to Increase COVID-19 Testing Access: Protocol for a Household Randomized Control Trial in Baltimore, MD

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Abstract

Background: The COVID-19 pandemic disproportionately affected low-income, and racial and ethnic minority populations. Testing plays a critical role in disrupting disease transmission, but complex barriers prevent optimal testing access, particularly for Black and Latinx communities. There is limited evidence on optimal testing modalities to increase testing access for these populations.

Objective: The primary objective of the Community Collaboration to Combat COVID-19 (C-FORWARD) trial is to define optimal COVID-19 testing modalities for maximizing testing acceptance, uptake, and timeliness of results receipt.

Methods: C-FORWARD is a household-randomized comparative effectiveness trial conducted in an urban population representative sample. Households across 653 census block groups were sampled using a probability proportional to size approach. The primary outcome was the completion of SARS-COV-2/COVID-19 testing within 30 days of randomization.

Results: Between February 2021 and December 2022. 1,083 individuals (881 index participants and 202 household members) were enrolled. The mean age of participants was 51 (SD ±18) years. Forty-three percent of participants identified as Black or African American, 48.6% as white, and 9.0% as other, including Asian, American Indian, Native Hawaiian or Pacific Islander, and multiple races. Five percent of participants identified as Hispanic or Latino. At the time of enrollment, 51.1% were currently working either full or part-time and 32.9% of participants had an advanced degree. Eighty percent of participants had been tested for COVID-19 previously, with 22.3% reporting having previously tested positive for COVID-19, and 86.8% of participants reported receiving at least one COVID-19 vaccination prior to enrollment.

Conclusions: Data from the C-FORWARD trial will be used to address important questions regarding COVID-19 testing acceptance and uptake in an urban population. Clinical Trial: Clinical Trials.gov ID: NCT04673292

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Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement: This study was approved by the Johns Hopkins University Institutional Review Board (IRB)

under IRB00250298.

Abstract

Background: The COVID-19 pandemic disproportionately affected low-income, and racial and ethnic minority populations. Testing plays a critical role in disrupting disease transmission, but complex barriers prevent optimal testing access, particularly for Black and Latinx communities. There is limited evidence on optimal testing modalities to increase testing access for these populations.

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Conclusions: Data from the C-FORWARD trial will be used to address important questions regarding COVID-19 testing acceptance and uptake in an urban population.

Key Words: infectious disease, SARS-CoV-2, COVID-19, disease control

Introduction

Background

The novel Severe Acute Respiratory Syndrome Coronavirus 2019 (SARS-CoV-2 or COVID-19) emerged as a new viral infection in December 2019. Now a global pandemic, as of December 2023, COVID-19 has infected over 100 million people in the United States and more than 1.1 million have died.[1] COVID-19 related morbidity and mortality has disproportionately affected low-income, and racial and ethnic minority populations.[2] While highly effective SARS-CoV-2 vaccines are widely available, multiple challenges have prevented optimal vaccine uptake, including vaccine hesitancy and misinformation, breakthrough infections, and emergence of new variants potentially impacting the effectiveness of the vaccine. Non-pharmaceutical interventions such as masking, testing, and social distancing therefore remain critical to controlling the pandemic.[3]

Testing plays a crucial role in preventing transmission. Early access to testing breaks infectious disease transmission chains and reduces contact between infected and susceptible persons, particularly with the high prevalence of asymptomatic and mild disease. Early testing can also reduce COVID-19 severity, as early case identification decreases time to treatment for infected individuals.[4] Currently there are a variety of tests available for COVID-19 testing, including PCR, antigen tests, and serum-based antibody tests.[5] Access to testing may also be limited by geographic areas with low testing access, i.e., “testing deserts.” Geographic areas with low rates of access to and availability of SARS-CoV-2 testing stem from an overwhelmed supply chain and a disjointed public health system. Jurisdictions have identified testing deserts in lower-income, highly segregated.[6] In 2021, rapid ‘at-home’ antigen tests became available for purchase by the general public. In theory, this should make testing more accessible at the population level, however during infection surges tests including ‘at-home’ antigen tests were often unavailable. Additionally access to at-home tests is dependent on being able to access stores, pharmacies, or other distributors of the at-home tests, which may be difficult in areas with limited access.

There are complex multilevel barriers to optimal testing (**Figure 1**), and the pandemic has put into stark relief social and structural determinants, leading to health inequities in testing. Evidence suggests that impoverished and minority populations experience increased barriers to testing. Latinx and Black communities are almost three and two times more likely to be uninsured compared to non-Latinx whites, respectively.[8] Blacks of all ages are also more likely to report not being able to see a doctor in the past year because of cost, which has direct implications for access to testing.[9] In addition, longstanding issues of institutional (i.e., medical, research, public health) racism resulting in mistrust and distrust, language barriers, and the cost associated with missing work all decrease the likelihood of testing among these subgroups. Exacerbating the disparity in testing access, Blacks also experience a higher burden of disease for many chronic conditions associated with COVID-19 (e.g., diabetes, hypertension, chronic obstructive pulmonary disease), placing them at increased risk of severe COVID-19 illness and mortality.[2]

Objective

The overall goal of the Community Collaboration to Combat COVID-19 (C-FORWARD) trial was to develop evidence related to COVID-19 testing for translation to public health control strategies. To define optimal COVID-19 testing modalities for maximizing testing acceptance, uptake, and timeliness of results, we implemented a household-randomized comparative effectiveness trial in an urban population representative sample. Secondary objectives were to determine multilevel (socioeconomic, behavioral) barriers and facilitators to SARS-CoV-2 testing and evaluate the impact of testing modality and receipt of positive results on subsequent testing behavior.

Methods

C-FORWARD is a household-randomized comparative effectiveness trial evaluating three COVID-19 testing modalities to identify optimal testing modalities among a population representative sample of households in Baltimore City, MD. The trial was conducted from February 2021 to June 2023. **Figure 2** shows the C-Forward project study schema illustrating the flow of enrollment from the initial survey to testing to final trial visit.

The trial has been registered at clinicaltrials.gov (NCT04673292) and the protocol follows recommendations for reporting from the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013 Statement.[7] Results will be reported in accordance with standards described in the Consolidated Standard of Reporting Trials (CONSORT) statement and CONSORT extensions for non-pharmacologic trials, cluster trials, and the draft extension for RCTs conducted using cohorts and routinely collected health data, which is forthcoming.

Setting

Baltimore City is a hyper-segregated city with white, Black, and Latinx residents, as well as high and low poverty communities, living in physically clustered, geographically isolated communities.[8] In Baltimore, Blacks have a median household income that is 54% of whites. Black residents make up more than 60% of the population yet more than twice as many Black families as white families live in liquid asset poverty, meaning they do not have sufficient savings to subsist at the poverty level for three months in the absence of income.[9]

Study population and Sampling strategy

The target population included English- and Spanish-speaking households residing in 653 census block groups

(CBGs) which we refer to as neighborhoods. We estimate that the target population comprised approximately 593,490 persons and 238,436 households living in the 653 CBGs in 2020.

The sampling selection for the study was conducted in two stages. In the first stage, among the 653 CBGs in Baltimore City, a sample of 105 census block groups was selected using a stratified, systematic probability proportional to size sampling strategy. The sample was selected from nine strata to ensure recruitment and enrollment of Latinx and Black populations; the strata were defined by poverty (>20% (vs. <20%) the household Federal poverty level) and race/ethnicity (>50% Non-Hispanic white, > 50% Non-Hispanic Black, >40% Latinx) [10] (Figure 3). In the second sampling stage, a total of 33,269 household addresses were provided by a vendor who receives updated sampling annually with USPS data on valid household addresses. Of the 33,269 households in the second stage sampling frame, 7.5% (2495) were fielded and of these, 96.6% (2411) households were successfully screened. During the screening, 93.0% (2,243) had at least one English- or Spanish-speaking person between the ages of 18 to 99.

Inclusion and exclusion criteria

Textbox 1 presents the inclusion and exclusion criteria for C-FORWARD participants. Households had to be one of the selected addresses in Baltimore City and have at least one household member 18 years or older who speaks English and/or Spanish who was psychologically fit to complete the survey (i.e., household index). The first household member 18 years or older to consent and enroll in the study was defined as the household index. After enrollment and completion of the baseline survey, the index was invited to enroll in the RCT, along with any other eligible household members.

Additional individual household member participants enrolled in the RCT were 5 years or older, report residence within the sampled household and speak English and/or Spanish and resided within a household of an index participant. Individual household members were excluded if they are a resident of a nursing home, half-way house, shelter, or do not reside at the selected household address. Individuals psychologically unfit to complete surveys, under the influence of illicit substance, or under the age of 5 years were excluded.

Textbox 1.

Inclusion criteria for households

1. Selected address within Baltimore City
2. At least one member of the household >18 years of age who speaks English and/or Spanish
3. At least one member of the household provides informed consent
4. At least one member of the household psychologically fit to complete survey

Exclusion criteria for households:

1. Adult member of the household is under the influence of illicit substances, in the opinion of the phone interviewer
2. Residents of nursing homes, half-ways houses or shelters
3. Psychologically unfit to complete the survey
4. Not a selected household address

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consent and baseline survey was also included in each letter mailed to households, along with a stamped and pre-addressed envelope to return the completed consent and baseline survey.

All recruitment materials (website, postcards, letters, door hangers), trial documents (informed consent and surveys) and patient education materials were offered in English and Spanish. For Spanish speaking participants, all trial visits and communication (visit scheduling, appointment reminders, results review) were offered in Spanish.

Informed Consent and Enrollment

Trial staff obtained informed consent and conducted surveys for each participant in their preferred language (English or Spanish), with assent obtained from capable children as necessary. One individual from each household (index) was consented and enrolled. At the time of consent, the household was randomized to one of three testing arms and the testing visit was scheduled.

All index household participants were eligible to enroll in the RCT. Research staff also asked for permission to contact any other household member(s) (identified in the household inventory) to ascertain their interest and willingness to participate in the trial. For willing households, research staff collected contact information for all household members and documented the permission to contact. Unwilling households were informed that other household members could be referred to the trial at any time.

RCT enrollment for the household index either continued immediately after completion of the survey (if the participant was willing) or at a later mutually agreed upon day/time. The informed consent for the RCT was provided to the household member participant via a website address/link (online via text or email). If the index participant was interested in enrolling in the RCT, but did not have access to the internet, a hard copy of the consent was mailed and enrollment took place at a later date. After receipt of the consent form, the trial staff member reviewed the consent form via the phone to ensure the participant provided an informed consent. The trial staff member electronically signed the consent form reflecting oral consent to 1) participation in the RCT; 2) consent for storage of biospecimens; 3) consent for additional genetic studies; 4) consent for future contact; 5) consent for Chesapeake Regional Information System for Patients (CRISP) medical record review;

and 6) consent for sharing zip code with Duke Clinical Research Institute (DCRI).

The same consent form shared with the household index was shared with all other household members who were 18 years of age or older. The same processes followed in the survey for obtaining informed consent were followed. RCT enrollment consisted of a survey for other enrolling household member participants, and for all household participants, testing according to household randomization assignment (see Trial Arms), the collection of host genetics and the storage of biospecimens. In addition, each participant was given phone numbers of the PI and the IRB office to contact if they had additional questions or concerns.

Questionnaires

Participants were asked about sociodemographic and health-related information in self-administered online or phone-administered surveys, depending on participant preference. Sociodemographic characteristics included age, race and ethnicity, sexual orientation, education, employment status, and relationship status. Health-related information included the presence of chronic health conditions and health-care-seeking behaviors. Questions were also included on social distancing and COVID-19 prevention behaviors, and previous COVID-19 symptoms, testing and results, and vaccination

Randomization

Randomization occurred at the household level. Once any adult household member enrolled in the RCT, randomization to one of the three testing modalities occurred using an individual-level stratified blocked randomization approach, stratified by geographic group and race/ethnicity (non-Hispanic white including Non-Hispanic Other, non-Hispanic Black, Hispanic/Latinx). The CBGs (n=105) selected as a part of the sampling strategy were classified into 12 strata according to geography. Stratum-specific (n=12) allocation sequences were generated per race/ethnicity/poverty (n=8) for a total of 96 strata. The sequences were integrated into REDCap using varying blocks sizes of 3 and 6 and households allocated at a 1:1:1 ratio to each testing modality. Household level randomization applied to all members of the household who agreed to participate in the RCT.

Study Arms

The enrollment target was 1,386 households randomized 1:1:1 to one of three SARS-CoV-2 PCR and antibody testing modalities (**Table 1**): Arm 1) fixed ambulatory outdoor testing site standard of care testing; Arm 2) community-based mobile van testing; or Arm 3) self-collected, home-based testing. A full description of tests is listed in **Figure 3.**

Fixed Site (Arm 1): This arm was designed to replicate standard of care (SOC) and included all three Johns Hopkins Medical Institution (JHMI) ambulatory outdoor testing sites across Baltimore City. Each testing site

represented a traditional appointment-based scheduling system. Participants were given a choice of one of three outdoor testing locations based on their preferences. Trial staff made appointments for testing based on testing availability and participant schedule.

Community-based mobile van testing (Arm 2): This arm offered the convenience of highly accessible testing, in close geographic proximity, and with the flexibility of no fixed appointment time. Each of the 12 geographic strata (see randomization) had a single, centrally located testing site within the area, providing similar geographic access across households.

Home Based Testing (Arm 3): Individuals in this arm received a home-based testing kit delivered to the household by a courier service. The testing kit included a Becton Dickinson swab for SARS-CoV-2 PCR testing, a Tasso device for the collection of 5mL of blood, and an Oracol swab for saliva collection. Easy to use instructions with options to view pre-recorded videos and/or virtual ‘on demand’ coaching sessions with members of the study team were available to the participant.

Table 1. Summary of Testing Modalities

Testing Modality	Location	Modality scheduling differences	Modality logistical differences	Laboratory Sample Type
Arm 1 Fixed site, standard of care	Johns Hopkins Health System testing sites	Participants select 1 of 3 sites and follow appointment schedule	Set time, fixed site, but may be inconvenient location and schedule	Nasal swab, NP swab, saliva, venipuncture
Arm 2 Mobile van	Central location within CBG	Participants arrange testing at a single testing van site in their CBG anytime by day, not time	Crowding and long-wait if all individuals come at the same time; but highly convenient	Nasal swab, NP swab, saliva, venipuncture
Arm 3 Home-based self-collection	Participants' home	Both nasal swab and saliva are delivered to participants via courier service. Participants completed 1 shipping requirement for two packages that will be sent back.	Most convenient, but self-sampling can lead to specimen errors; delay or failure to return sample in mail is costly and no results	Nasal swab, saliva For those enrolling prior to December 10, 2021: blood self-collection device

Study

Changes

Due to the unprecedented and ever-evolving nature of the COVID-19 pandemic, several changes to study design were implemented over the course of the study. These changes were necessary to continue the trial and we do not believe these changes impacted the validity of the trial. The changes are documented in **Table 2**.

Table 2. Study Changes Implemented Across the Span of C-Forward.

Change	Date Implemented	Affected Testing Modalities	Description

Change from three to two fixed testing sites	June 2021	Arm 1 Fixed site, standard of care	One Johns Hopkins Health System testing sites closed in June 2021, resulting in two fixed testing sites instead of three
Removal of blood self-collection device for home-based collection	December 2021	Arm 3 Home-based self-collection	The Tasso blood self-collection device was removed from the home-based testing. This eliminated serum-based antibody testing from the home-based testing participants.
Change length of follow-up from 12-months to 6-months	January 2022	All Study Arms	The length of follow-up for the study was changed from 12-months to 6-months, resulting in a total of 6 possible monthly visits instead of 12.
Change from self-administered swab packaged by and returned to Johns Hopkins laboratory to Everlywell™ home testing kit	January 2022	Arm 3 Home-based self-collection	Arm 3 home testing kit changed from a self-administered swab returned to Hopkins laboratory to the PCR kit will include provisions for the shipping of samples directly to a company called, Everlywell, via UPS dropbox and/or fixed UPS location.
Change household member eligibility from 5 years old to 16 years old.	January 2022	All Arms	Due to the switch to the Everlywell™ testing kit, participants under the age of 16 could not be tested

			using the home-based collection. Due to this, eligibility across all arms was updated to 16 years.

Study Outcomes

The primary outcome was completion of SARS-CoV-2 testing, defined as the proportion of RCT consented participants who complete SARS-CoV-2 testing within 30 days of consent/randomization (**Table 3**). Completion of SARS-CoV-2 testing was defined as the completion of SARS-CoV-2 PCR testing at the testing site (for fixed site arm and mobile van) or the return of PCR swab by the participant to the lab via the courier service. After consent, participants were scheduled for testing visit at their randomized testing modality. Trial staff made up to 10 attempts to schedule a participant for testing. Participants were allowed to reschedule their testing visit up to 3 times.

Secondary outcomes (**Table 3**) included time (in days) to completion of SARS-CoV-2 PCR testing, receipt of SARS-CoV-2 PCR test results within 30 days of consent, and time from SARS-CoV-2 PCR test to receipt of SARS-CoV-2 PCR test results among those who receive test results. SARS-CoV-2 results were communicated to the participant by trial staff or through EMR messaging (EPIC MyChart).

Table 3. Primary and Secondary Outcomes for the C-Forward Trial.

Outcome	Primary or Secondary	Definition
Completion of SARS-CoV-2 testing	Primary	The proportion of RCT consented participants who complete SARS-CoV-2 testing within 30 days of consent/randomization. Completion of SARS-CoV-2 testing was defined as the completion of SARS-CoV-2 PCR testing at the testing site (for fixed site arm and mobile van) or the return of PCR swab by the participant to the lab via the courier service
Time (in days) to completion of SARS-CoV-2 PCR testing	Secondary	Number of days from consent/randomization date to the date of SARS-CoV-2 PCR testing at the testing site (for fixed site arm and mobile van) or the return of PCR swab
Time (in days) from SARS-CoV-2 PCR test to receipt of SARS-CoV-2 PCR test results among	Secondary	Number of days from consent/randomization date to the date of SARS-CoV-2 PCR testing results were communicated to the participant by trial staff or through EMR messaging (EPIC MyChart).

those who receive test results		

Sample size/Power considerations

We calculated power for comparing the primary outcome related to randomization (proportion who complete SARS-CoV-2 testing) across arms (Arm 3 vs. Arm 1 and Arm 2 vs. Arm 1). Given that we enroll 1,386 households in the three arms, and that we randomized at the household level, we will be able to detect a difference in the level of testing in Arms 2 or 3 and the control arm (Arm 1) of approximately 11%, (from 50% in the control arm to 61% in the comparison arm) with at least 80% power. We assumed an overall type one error of 0.05, and controlled for multiple comparisons using a Bonferonni correction. Testing for individuals in the same household may be highly correlated, and so we conservatively assumed that each household only enrolls one individual. This detectable difference of 11% corresponds to a prevalence ratio of 1.2 given that testing prevalence is 50% in the control arm, to as low as 1.17, for a testing prevalence of 70% in the control arm.

Planned Analyses

We hypothesize that compared to the SOC arm, those randomized to the community-based, mobile van testing arm (Arm 2) and the self-collection, home-based testing arm (Arm 3) will be more likely to receive a COVID-19 PCR test than those assigned to the SOC arm (Arm 1).

Primary analyses

The primary analysis will use an intention-to-treat approach only among index participants. Assuming one participant enrollment per household, a Poisson regression will be used to calculate prevalence ratios comparing the effect of each of the two testing modalities (mobile van testing, home-based testing) vs. the SOC (fixed-site testing) on the primary outcome of interest, the proportion receiving a test within 30 days. Because of randomization, we assume that factors salient to testing access will be balanced across arms and proportions will be directly comparable without adjustment. However, we will assess whether confounding by key baseline factors is present (e.g., age, sex, race/ethnicity) and will complete adjusted analyses accordingly.

Secondary analyses

In addition to comparing the proportion of index participants who received a SARS-CoV-2 PCR test within thirty days, we will also examine the time until the first SARS-CoV-2 PCR test using time to event analysis among index participants (one per household). We will measure the time for each participant from enrollment until the first testing event occurs.

Each participant's time until testing will be censored when the participant exits the study. We will use Cox proportional hazards to compare the rate of testing between arms and whether those in the mobile testing arm (Arm 2) or the home-based testing arm (Arm 3) tend to be tested earlier or later than those in SOC arm. As for primary analysis, due to the randomization, we expect that participants will be similar across arms, however we will consider adjusting for demographic factors or characteristics that are not balanced across arms.

We will also examine the secondary outcome of receipt of SARS-CoV-2 PCR test results within 30 days of the RCT consent as a percent of trial participants in each arm. In order to compare this secondary outcome between arms, we will use Poisson regression to estimate the prevalence ratios between Arm 2 and 3 relative to the SOC arm (Arm 1). Consistent with our analysis for the primary outcome, we will adjust for baseline factors if they appear different between the arms at baseline.

We will examine two additional secondary outcomes among study participants, (1) time from SARS-CoV-2 PCR test to receipt of SARS-CoV-2 PCR test results, and (2) time from consent to receipt of SARS-CoV-2 PCR test results, both of which will be compared between arms using time to event analysis with Cox proportional hazards, consistent with the analysis for time from enrollment until the first SARS-CoV-2 PCR test. Participants who do not complete a SARS-COV-2 PCR test during the study period will still contribute to analyses of these secondary outcomes as having censored event times, so this analysis will be among all participants.

We will also examine effect modification for a selection of demographic characteristics by repeating the analysis of primary and secondary outcomes as specified above within specific strata, including (1) race/ethnicity (Black, Latinx, white), (2) gender, (3) neighborhood poverty (households in CBG with more than 20% of households below the federal poverty line and households in CBG with less than 20% of households below the federal poverty line), (4) household poverty (5) essential worker status, (6) exposure or symptoms and (7) vaccination and (8) age, (9) education (high school diploma or not) (10) household size (with threshold at median).

Primary and secondary analyses will be among index participants so that only one participant per household is included. We will repeat these analyses including all participants and accounting for clustering within household, using GEE for Poisson regression and a robust variance estimator for Cox proportional hazards.

Since household members are appreciably different from the index participants because they are enrolled after randomization is complete and thus their decision to participate and motivation for testing might be influenced by the randomization arm. Thus, additional secondary outcomes will examine testing uptake and completion

among household members only.

Results

C-FORWARD enrollment began on February 25, 2021, and concluded on November 23, 2022: a total of 1,083 individuals (881 index participants and 202 household members) were enrolled. The mean age of participants was 51 (SD ±18) years and ranged from 5 to 98 years. Overall, 42.5% of participants identified as Black or African American, 48.6% as white, 3.4% as multiple races, 2.7% as Asian, and 2.9% as another race, while 4.8% identified as Hispanic or Latino. The majority of participants (51.1%) were currently working either full or part-time at time of enrollment. Approximately 32.9% of participants had an advanced degree.

At time of enrollment, over three quarters (79.9%) of participants had been tested for COVID-19 previously, with 22.3% reporting having previously tested positive for COVID-19. 86.8% of participants reported receiving at least one COVID-19 vaccination prior to enrollment.

Table 4. Selected Baseline Characteristics of Participants Enrolled in C-FORWARD (n=1083).

Characteristics	Overall (n =1083)	
Number of Households, n	881	
Age, Mean (SD)	51 (18)	
	n	%
Sex, Male	380	(35.1)
Race		
Black or African American	460	(42.5)
White	526	(48.6)
Multiple races	37	(3.4)
Asian	29	(2.7)
Other	31	(2.9)
Ethnicity, Hispanic or Latino (n=1006)	48	(4.8)
Employment		
Working now (either full time or part time)	553	(51.1)
Retired/Disabled/Keeping house	384	(35.5)
Student	64	(5.9)
Looking for work, Unemployed	53	(4.9)
Essential Worker		
Among enrolled adults with responses (n = 972)		
Essential Worker	241	(24.8)
Educational Attainment (n=1038)		
High School Graduate or less	264	(25.4)

Some college level/Technical/Vocational degree/ Associate's degree	223	(21.5)
Bachelor's degree	201	(19.4)
Other Advanced degree	342	(32.9)
Health Insurance (n=854)		
No health insurance	29	(3.4)
Public (Medicare, Medicaid, Tricare)	376	(44.0)
Private (purchased directly or through employment)	420	(49.2)
Ever been tested for COVID-19? (self-report, n=1013)	809	(79.9)
Ever tested positive for COVID-19? (self-report, n=804)	179	(22.3)
COVID-19 vaccination (self-report, n=1025), at least one dose	890	(86.8)

Discussion

This trial will provide critical information on best practices for SARS-CoV-2 testing in communities with a high prevalence of vulnerable populations. Beyond increasing our understanding of SARS-CoV-2 testing, this study will help to characterize the prevalence of COVID-19 infection. Even with expanding access to pharmaceutical interventions, COVID-19 testing remains crucial to control. Testing strategies must be well studied to determine the most effective and accessible strategies to inform public policy and public health prevention and control activities. The C-FORWARD trial will provide critically needed insights into optimal testing strategies, particularly for vulnerable populations most affected by a pandemic.

There were several implementation-related challenges confronted during the C-FORWARD trial. Given the ever-changing pandemic landscape and region-specific surges in COVID-19 incidence, testing demand was often both sporadic and urgent. The emergence of new variants also resulted in the current SOC being chaotic which varied by testing location, even within the same city, making it difficult to have a true comparison arm.

Temporal trends in the SOC delivery approach over the duration of the trial affected our ability to draw comparisons between the fixed site and other testing modalities. However, our ongoing ethnographic work and community engagement will capture these changes so that we can address them in the analysis as appropriate (e.g., stratifying by time period). It was also possible that randomized households/ individuals

sought testing outside of the study,

Furthermore, responses to surveys are subject social desirability and recall basis; moreover, recall may be influenced by prior COVID-19 infection status, which is one of the key exposures of interest. We will use 2-week time frames for most behaviors to minimize this effect. Loss to follow-up is another concern, particularly as attitudes toward COVID-19 change, and fatigue with study participation may set in.

As early and accessible testing can prevent forward transmission and improve individual-level outcomes, this trial aims to identify the most effective approach with which to provide access to COVID-19 testing. In addition to improving our understanding of how testing modality affects access and effectiveness of testing initiatives, this work focuses on access within populations having the highest burden of COVID-19 disease and thus who will benefit most from these findings.

Study Figures

Figure 1. Anderson's Behavioral Model for Vulnerable Populations, the Conceptual Framework of SARS-CoV-2 testing utilization based on Behavioral Model of Access to Care.

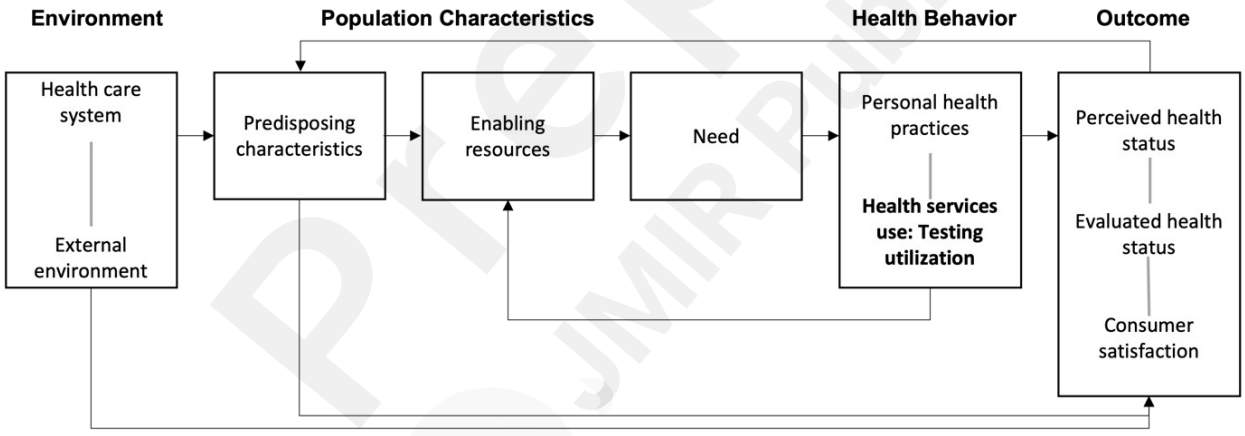


Figure 2. Project Schema

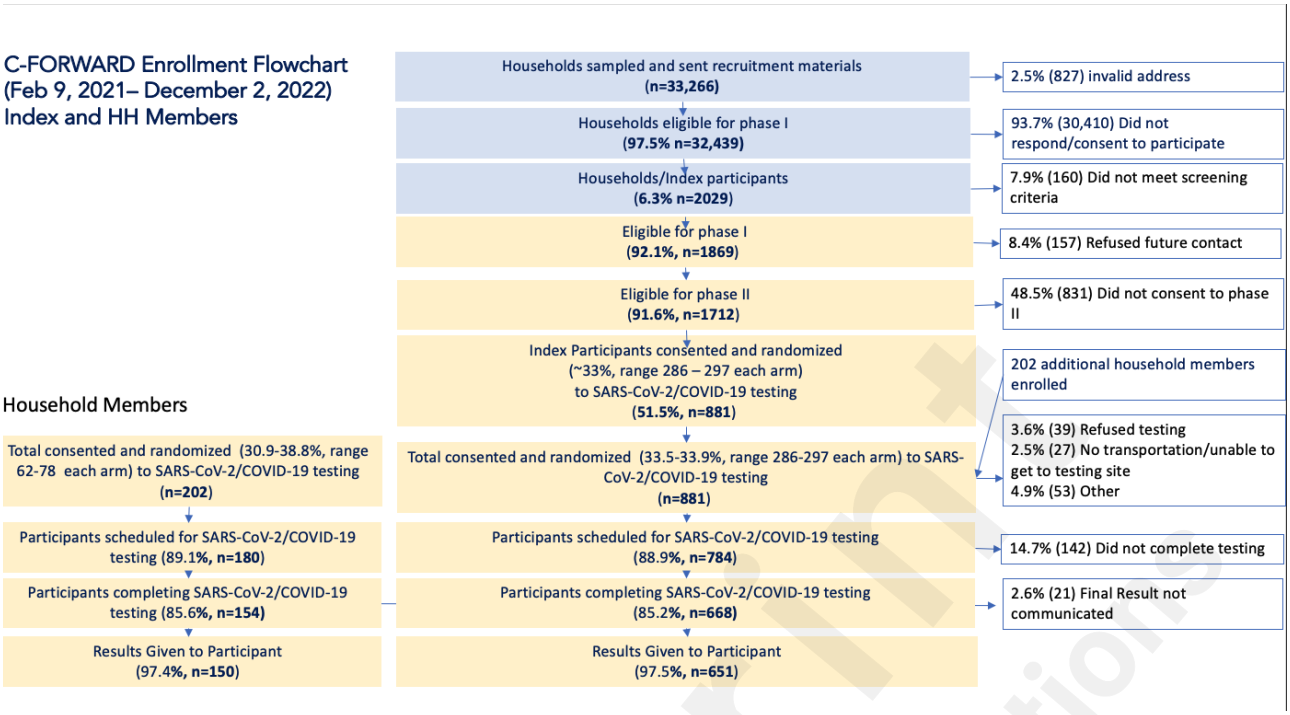


Figure 3. Biological Samples and Laboratory Testing by Trial Arm

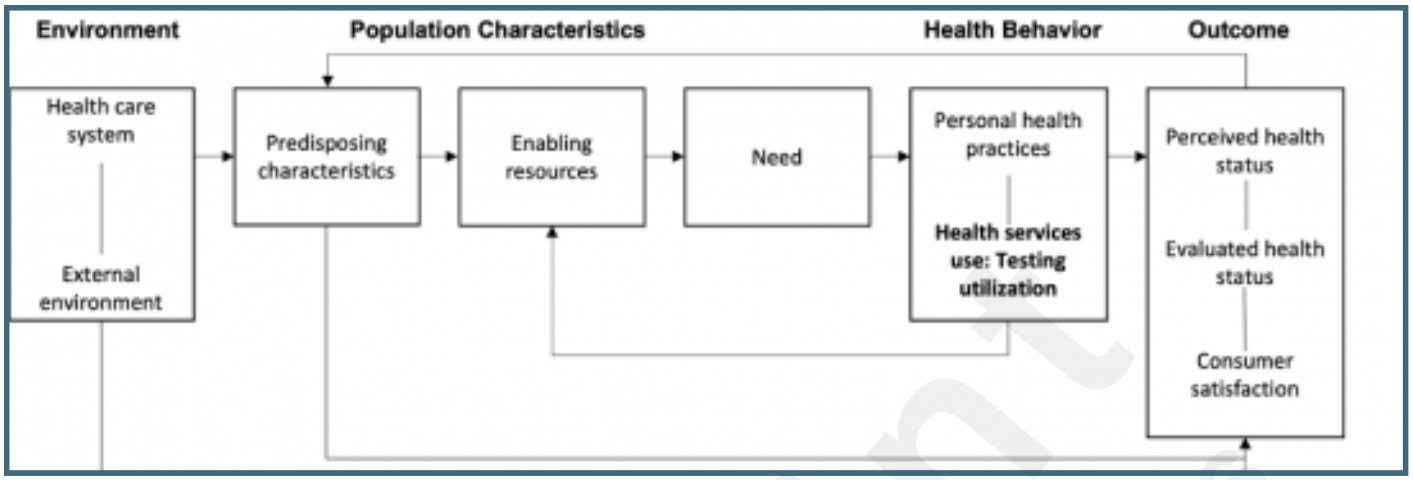
Testing	Baseline	Weekly	Month 1 - 5	Month 6	Interim Testing Visit
Standardized COVID-19 education	X			X	X
Verification of symptoms and clinical presentation	X			X	X
Contact identification (if symptomatic)	X			X	X
Temperature and pulse oximetry	X			X	X
ARM 1 / ARM 2 (laboratory Testing-blood)					
CBC with differential and platelets	X			X	X
Hepatic Function Panel (AST, ALT, total bilirubin, albumin, alkaline phosphatase)	X			X	X
Acute Phase Reactants – CRP, ESR, LDH + IL-6	X				X
Coagulation: D-Dimer	X				X
Creatinine	X				X
ARM 1 / ARM 2 (Specimens for Viral RNA/RT-PCR)					
Nasopharyngeal, Nasal, Middle Turbinate, and/or Oropharynx	X			X	X
Saliva	X			X	X
Antibody testing					
Serum antibody testing (IgM/IgA/IgG)	X			X	X
Saliva antibody testing	X			X	X
Repository specimens *(future studies)*					
Plasma for storage	X			X	X
PBMC for additional immunology testing	X			X	X
Host genomic testing (on stored blood via sub-study protocol)	X			X	X
ARM 3 (Home Self-Test Kit)					
Saliva Sponge	X			X	X
Tasso SST blood collection device	X			X	X
PCR Nasal Swab	X			X	X

Supplementary Files

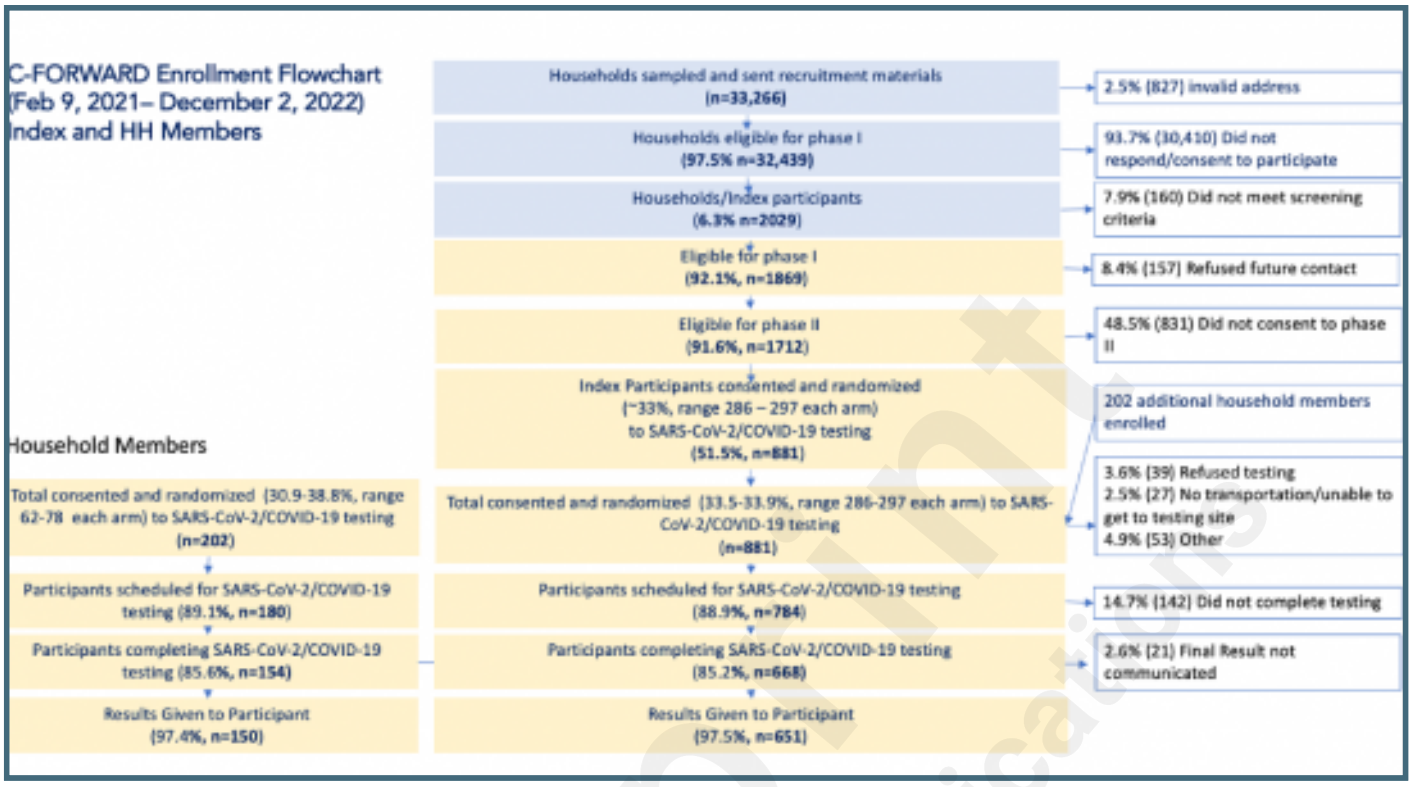
Updated manuscript.
URL: http://asset.jmir.pub/assets/1ac5ac845c89c77e7b600dd55f1ac183.docx

Figures

Anderson’s Behavioral Model for Vulnerable Populations, the Conceptual Framework of SARS-CoV-2 testing utilization based on Behavioral Model of Access to Care.



C-Forward Project Schema.



Biological Samples and Laboratory Testing by Trial Arm.

Testing	Baseline	Weekly	Month 1 - 5	Month 6	Interim Testing Visit
Standardized COVID-19 education	X			X	X
Verification of symptoms and clinical presentation	X			X	X
Contact identification (if symptomatic)	X			X	X
Temperature and pulse oximetry	X			X	X
ARM 1 / ARM 2 (laboratory Testing-blood)					
CBC with differential and platelets	X			X	X
Hepatic Function Panel (AST, ALT, total bilirubin, albumin, alkaline phosphatase)	X			X	X
Acute Phase Reactants – CRP, ESR, LDH + IL-6	X				X
Coagulation: D-Dimer	X				X
Creatinine	X				X
ARM 1 / ARM 2 (Specimens for Viral RNA/RT-PCR)					
Nasopharyngeal, Nasal, Middle Turbinate, and/or Oropharynx	X			X	X
Saliva	X			X	X
Antibody testing					
Serum antibody testing (IgM/IgA/IgG)	X			X	X
Saliva antibody testing	X			X	X
Repository specimens *(future studies)*					
Plasma for storage	X			X	X
PBMC for additional immunology testing	X			X	X
Host genomic testing (on stored blood via sub-study protocol)	X			X	X
ARM 3 (Home Self-Test Kit)					
Saliva Sponge	X			X	X
Tasso SST blood collection device	X			X	X
PCR Nasal Swab	X			X	X