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SCALE-UP II: Protocol for a Pragmatic Randomized Trial Examining Population Health Management Interventions to Increase the Uptake of At-Home COVID-19 Testing in Community Health Centers

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ABSTRACT

Introduction. SCALE-UP II aims to investigate the effectiveness of population health management interventions using text messaging (TM), chatbots, and patient navigation (PN) in increasing the uptake of at-home COVID-19 testing among patients in historically marginalized communities, specifically those receiving care at safety net community health centers (CHCs).

Methods and Analysis. The trial is a multi-site, individually randomized pragmatic clinical trial. Eligible patients will be ≥ 18 years old with a primary care visit in the last three years at one of the participating CHCs. Patient demographic data will be obtained from CHC electronic health records. Patients will be randomized to one of two factorial designs based on smartphone ownership. Patients who self-report replying to a text message that they have a smartphone will be randomized in a 2x2x2 factorial fashion to receive (i) chatbot or TM; (ii) PN (yes or no); and (iii) repeated offers to interact with the interventions every 10 or 30 days. Participants who do not self-report as having a smartphone will be randomized in a 2x2 factorial fashion to receive (i) TM with or without PN; and (ii) repeated offers every 10 or 30 days. The interventions will be sent in English or Spanish, with an option to reply requesting free at-home COVID-19 test kits. The primary outcome will be the proportion of participants using at-home COVID-19 tests during a 90-day follow-up. The study will evaluate main effects and interactions among interventions, implementation outcomes, and predictors and moderators of study outcomes. Statistical analyses will include logistic regression, stratified subgroup analyses, and adjustment for stratification factors.

Ethics and dissemination: The study protocol was approved by the University of Utah Institutional Review Board. On completion, study data will be made available in compliance with National Institutes of Health data sharing policies.

Trial registration: Clinicaltrials.gov (NCT05533918 and NCT05533359).

Keywords: COVID-19, digital health, health equity, population health management

Strengths and limitations of this study

- At-home COVID-19 testing is an important strategy to help reduce exposure and offer timely treatment to individuals at a higher risk for severe disease.
- The population health management interventions are scalable and will enable increasing the reach and uptake of at-home COVID-19 testing.
- Dissemination strategy modalities (i.e., voice and text cellphones) are nearly ubiquitous among adults in the United States, including among historically marginalized populations.
- Patient population will be drawn from community health centers in a single state.

INTRODUCTION

Racial/ethnic minority, low socioeconomic status (SES), and rural populations suffer profound health inequities across a wide variety of conditions, including a higher rate of hospitalization and mortality due to COVID-19.[1-4] Similar inequities have been found across the US for vaccination rates between urban and rural,[5] high and low SES,[6] and White and non-White populations.[7,8] Low vaccination rates and withdrawal of protection measures leave historically marginalized populations at high risk for local outbreaks and more contagious variants.

Although public health agencies worldwide have declared the end of the pandemic, timely testing is still important to help reduce exposure and offer timely treatment to individuals at a higher risk for severe disease. However, historically marginalized communities lacked easy and convenient access to testing throughout the COVID-19 pandemic, especially after the closure of mass test sites nationwide.[9,10] Although several FDA-approved at-home tests are available, providing a convenient, quick and low-cost alternative for patients to test at home,[11,12] substantial disparities exist in the use of at-home COVID-19 testing. While the use of at-home COVID-19 testing has more than tripled between the Delta and Omicron outbreaks, use of at-home testing was more than twice as high among individuals identifying as White, having high SES, and having a postgraduate degree.[13] Thus, scalable approaches are needed to promote the uptake of at-home COVID-19 testing among individuals from historically marginalized communities.

Despite evidence of a digital divide between high resource healthcare systems and low resource community health centers (CHCs),[14,15] historically marginalized populations have almost universal access to technology such as cellphones, which provide opportunities for large scale population health management (PHM) interventions. Even in households with annual incomes less than $30,000, 97% own a cellphone and 76% own a smartphone.[16] The SCALE-UP II trial will investigate three PHM interventions (text messaging [TM], automated chatbot, and patient navigation [PN]) to increase the reach and uptake of at-home COVID-19 testing among patients who receive care at CHCs.

METHODS AND ANALYSIS

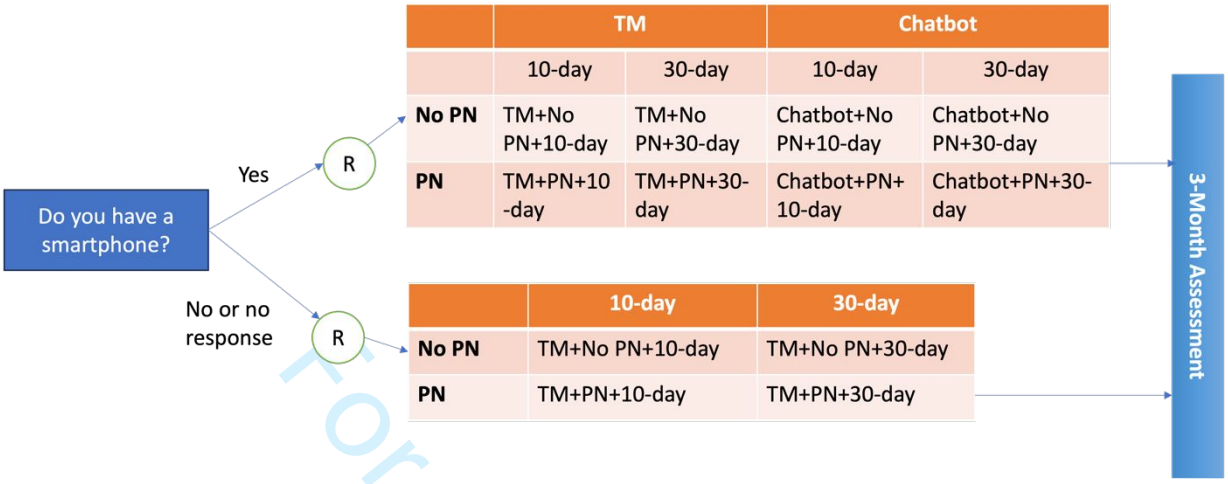
This protocol was developed using the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT).[17] The protocol was approved by the Institutional Review Board at the University of Utah on June 10, 2022 (IRB_00150669). The trial was registered with Clinicaltrials.gov (NCT05533918 and NCT05533359) on September 9, 2022. Enrollment was planned to begin in December 2022 and data collection was planned to end in November 2023.

Patient and Public Involvement

SCALE-UP II is conducted in partnership with the Association for Utah Community Health (AUCH), CHCs across Utah, the Utah Department of Health and Human Services (UDHHS), and the University of Utah. Our research-practice partnership uses a multi-pronged community engagement approach to (i) identify research questions, (ii) develop, adapt, and implement interventions, and (iii) inform dissemination plans.[18,19] The community engagement approach includes a weekly project meeting with AUCH, UDHHS, and the research team and quarterly Patient Advisory Committee (PAC; consisting of CHC patient representatives) and Study Advisory Committee (SAC; consisting of patients, CHC staff, UDHHS, and AUCH representatives) meetings. The research objectives of SCALE-UP II were identified in partnership with AUCH and UDHHS; both AUCH and UDHHS were interested in addressing the impact of COVID-19 among historically marginalized communities in Utah. Input from the PAC informed the design of the text messaging and chatbot interventions. Furthermore, TM and Chatbot scripts were developed following information gathered from community members in Utah.

Study Design

SCALE-UP II is an individually randomized, multi-site, pragmatic clinical trial. The experimental design varies according to each patient's response to a text message asking if they have a smartphone. Participants who self-report that they have a smartphone will be randomized in a 2x2x2 factorial fashion to receive (i) chatbot or TM; (ii) PN (yes or no); and (iii) repeated offers to interact with the interventions every 10 or 30 days. Participants who do not respond to the introductory text message or who self-report as not having a smartphone will be randomized in a 2x2 factorial fashion to receive (i) TM with or without PN; and (ii) repeated offers every 10 or 30 days.



R=randomization; PN=patient navigation; TM=text messaging

Figure 1 – SCALE-UP II Trial Design

Rationale for Study Design

The interventions in SCALE-UP II interventions leverage (i) wide adoption of electronic health record (EHR) systems, even in low resource CHCs;[20,21] (ii) wide adoption of cellphones with at least voice and text capabilities;[16] and (iii) the low cost, efficiency, and simplicity of at-home COVID-19 tests.[11,12] Therefore, SCALE-UP II is designed to maximize reach with low-cost interventions to increase the uptake of COVID-19 testing in historically marginalized communities.

SCALE-UP II will enroll patients from Utah CHCs. These settings provide primary care to diverse, low SES populations, and provide an ideal setting to address COVID-19 because there is an established relationship and coordination of care, and ~80% of individuals see a primary care provider at least annually.[22] Three Utah CHC systems and their 12 primary care clinics will participate in SCALE-UP II. Demographics of SCALE-UP II CHC patients include: 51% Latino, 62% ≤100% federal poverty level, 69% uninsured, and receiving care in clinics where 17% are in rural/frontier areas.[23]

Since the chatbot requires a smartphone with connection to the internet, and about 25% of individuals with low SES and from rural areas do not have a smartphone,[16] SCALE-UP II will enroll patients in one of two factorial designs based on their smartphone ownership in order to maximize reach to the 96% of individuals who own at least a voice and text cellphone.

Patients may be reluctant to test due to hesitancy and numerous other barriers.[24,25] However, practical advice from patient navigators such as community health workers can help overcome hesitancy and engagement barriers such as logistics, transportation, and expense; of critical importance, providers welcome the use of these approaches with their patients.[26-28] Thus, in addition to the TM and chatbot interventions, SCALE-UP II will examine the added effect of offering access to patient navigation upon request through either intervention. Since patient navigation is a human-intensive intervention, examining the uptake of patient navigation when provided only upon request is critical for conserving resources in limited resource settings such as CHCs.

Participants

The study inclusion criteria aim to enroll a broad range of individuals to maximize reach. Eligible patients will be those who (i) have been seen at one of the participating CHCs in the last three years, (ii) are 18 years and older, (iii) have a working cellphone listed in the CHC EHR, and (iv) indicate a language preference in the EHR of English or Spanish.

The study will exclude participants who opt out upon receipt of the introductory message asking about smartphone ownership. Also, if more than one patient shares the same smartphone number in the EHR, only the patient with the most recent documented clinical encounter will be included.

Recruitment

As a pragmatic trial with interventions that offer minimal risk, the University of Utah IRB approved a waiver of consent for randomization and receipt of PHM interventions. Therefore, all participants who meet eligibility criteria will be automatically enrolled in the study. All three study points of contact (TM, chatbot, PN) will allow participants to opt-out through a simple reply at any time. Participants will be consented to complete the 3-month follow-up survey prior to survey completion using a consent cover letter.

Randomization and Blinding

Participants who self-report having a smartphone will be randomized to one of eight study arms (Figure 1): (1) TM+10-day, (2) TM+30-day, (3) Chatbot+10-day, (4) Chatbot+30-day, (5) TM+PN+10-

day, (6) TM+PN+30-day, (7) Chatbot+PN+10-day, or (8) Chatbot+PN+30-day. Participants who do not self-report to have a smartphone will be randomized to one of four study arms: (1) TM+10-day, (2) TM+30-day, (3) TM+PN+10-day, or (4) TM+PN+30-day. Participants will be randomized after receiving the introductory text message asking if they have access to a smartphone.

Randomization will be implemented by software and will utilize randomized permuted blocks to guard against any biases due to ordering of patients. Furthermore, the randomization will be stratified by CHC and urban/rural designation of the participant's zip code according to rural-urban commuting area (RUCA) codes.

The study is outcome assessor and investigator blinded. Patient navigators cannot be blinded to treatment assignment. Participants will be blinded to study participation.

Study Interventions

Overall, all study interventions (i) are sent on behalf of the participant's clinic, (ii) offer the option to request at-home mailed COVID-19 test kits at no cost for use as needed, (iii) are provided automatically in English or Spanish based on the patient's preferred language in the CHC EHR, and (iv) provide an option for participants to opt-out at any time (see Figures 2 and 3).

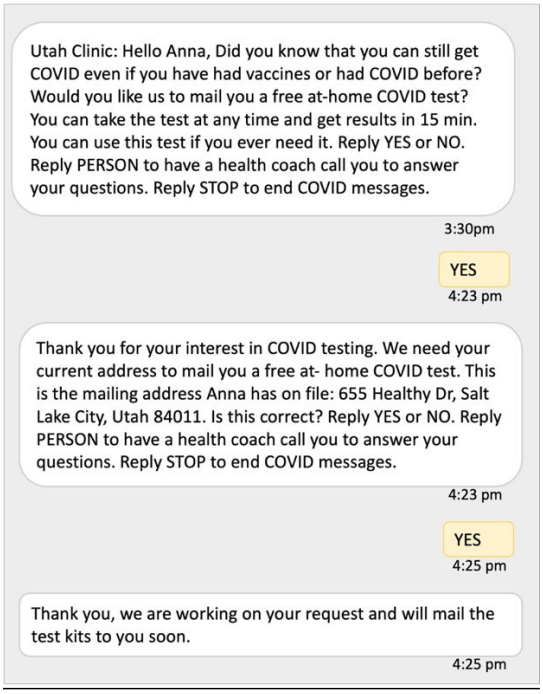


Figure 2 – Sample text message conversation offering COVID-19 at-home testing.

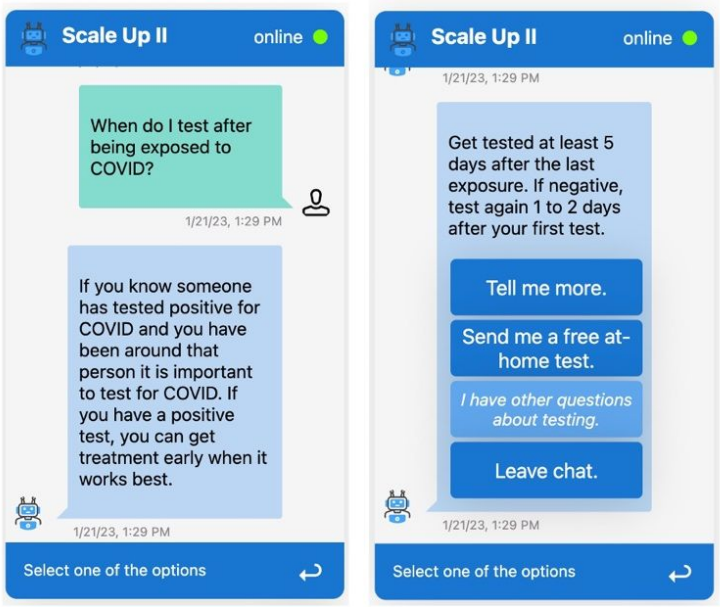


Figure 3 – Sequential screenshot of chatbot intervention showing a question being answered, followed by options to ask further questions, and request a COVID-19 test kit to be mailed to the patient's home.

Text Messaging (TM). Meta-analyses of text messaging interventions have found these approaches to be promising for improving compliance with healthy behaviors and preventive care, beneficial for multiple racial/ethnic groups, and inexpensive to deliver.[29-34] A US Department of Health and Human Services review concluded: *With the near-ubiquitous presence of cellphones and the rapid growth of smartphones, text messaging and other mHealth interventions can remove traditional geographic and economic barriers to access to health information and services. The higher rates of mobile phone ownership and use among Blacks and Hispanics, compared to Whites, are particularly noteworthy. These interventions have the potential to improve health knowledge, behaviors, and outcomes and, ultimately, to reduce disparities*.[34] Our own research has demonstrated that a simple, repeated offer to connect unmotivated, low-SES individuals with treatment resources resulted in 25% of individuals enrolling in tobacco cessation treatment.[35] Thus, repeated prompting offering access to COVID-19 testing via texts is an extremely convenient, low cost, scalable approach for increasing testing uptake.

TM will consist of bidirectional text messaging sent on behalf of the participant's clinic with a

response option for patients to request at-home mailed COVID-19 test kits at no cost (Figure 2). Participants randomized to TM+PN will also be able to reply requesting to speak with a patient navigator. Messages will be sent in English or Spanish based on the patient's language preference in the EHR.

Chatbot. Chatbots are automated conversational agents designed to mimic human interaction. Chatbots are increasingly popular in various health contexts as they can be easily accessed through smartphones, tablets, laptops, or desktops. Chatbots have many advantages for patient engagement, including providing scripted education interactively, chunking information into small segments that are easier to process, and allowing for choice in the amount of information received. Chatbots are accessible to the vast majority of U.S. adults. Even in households with annual incomes less than $30,000, 76% own a smartphone.[16,36,37] Delivery of health services through chatbots in research contexts has been successfully tested in various health domains such as mental health, asthma, diabetes management, and physical activity uptake.[38] While scripted chatbots have been widely used in the COVID-19 pandemic, especially to evaluate patient's eligibility for testing and vaccination,[39-44] research is needed to examine their benefits in addressing COVID-19 at-home testing. In addition, there is a lack of studies that investigated the design and implementation of chatbots specifically for historically marginalized populations.

For SCALE-UP II, we designed a scripted chatbot (i.e., predefined conversation script, and a fixed set of questions and scripted answers) that presents participants with a list of topics that address most common knowledge gaps and hesitancy factors related to at-home COVID-19 testing (Figure 3). The chatbot script was designed and guided by findings from a national survey and in-depth interviews with participants in the targeted Utah population, both conducted by our team. The following topics are covered: benefits of testing (even when already vaccinated or previously had COVID), when to test, test accuracy, how to use a test, and what to do if a test is positive.

Patients in the chatbot condition will receive a text message on behalf of their clinic offering a hyperlink to access the chatbot on the phone's web browser. At any point in the chatbot, participants will be able to click a button to request an at-home test kit. Participants randomized to the PN condition can

also click PERSON to request to speak to a patient navigator. As in TM, the chatbot is offered both in English and Spanish.

Patient Navigation (PN). SCALE-UP II will use community health workers (CHWs) employed by AUCH as patient navigators to address practical barriers, motivation, and hesitancy to COVID-19 testing. To assist navigators in working with patients, CHWs will be trained in an empirically-validated behavior change approach (Motivation And Problem Solving; MAPS).[45-50] MAPS is a holistic, dynamic approach to behavior change that integrates two empirically validated approaches (motivational interviewing[51,52] and practical problem solving[47,53,54]) for helping patients engage in target behaviors.[45-47,49,50] Importantly, MAPS addresses patients' social determinants of health, and provides practical advice and connections to services whenever possible, including addressing testing concerns (e.g., worries about repercussions of a positive test, infecting family members, quarantining, financial). MAPS has been demonstrated to be effective in numerous randomized controlled trials with respect to increasing enrollment in evidence-based interventions, as well as enhancing and maintaining behavior change.[45-47,49,50]

All SCALE-UP II navigators will receive ~20 hours of training, consistent with recommended training for helpline specialists.[55] Participants randomized to the PN condition who request to speak with a patient navigator will receive a phone call within 48 hours. Patient navigators will make three attempts to contact a participant.

Study Roll-Out Schedule

To ensure that the interventions work properly with real patient data, a pilot study will be conducted with a random sample of patients from one of the participating CHCs both for the TM and Chatbot interventions.

For the remainder of patients, to address bottlenecks that depend on non-automated processes (e.g., mailing of test kits, patient navigation), study participants will be exposed to interventions in one of 14 weekly batches according to a pre-defined schedule, in which a cohort with a new set of participants is added to the study every week. Participants will be randomly allocated across the 14 batches, also

stratified by CHC and urban vs. rural.

Every cycle starts by sending the introductory message to participants in the cohort (Day -2). Participants will have two days to respond. After that, eligible participants will be randomized into one of the two factorial designs depending on their response to the introductory message (Day 0). After randomization, participants will receive messages offering access to at-home testing once every 10 versus 30 days for 7 weeks (Days 0, 10, 20, 30, 40, 50, and 60 vs. Days 0, 30, and 60).

Outcome Assessment

The main study outcomes are described below. Table 1 provides a complete list including the primary, secondary outcomes, and implementation outcomes, as well as predictors and moderators of study outcomes.

Primary Outcomes and Hypotheses. The primary outcome is *Testing*; the proportion of study participants who use an at-home COVID-19 test during the course of 90-day study follow-up as defined below. For all patients, regardless of self-report of smartphone ownership, the primary hypotheses are main effects for PN (PN > No PN), main effects for message frequency (10-day > 30-day), and that TM+PN will lead to higher *Testing* than TM. These hypotheses will be tested at an alpha of .0167, adjusted for multiple comparisons using the Bonferroni method. Because we anticipate a low sample size of smartphone self-reporters to be adequately powered, we consider Chatbot-related hypotheses as secondary. These include the hypothesis that Chatbot will lead to a higher *Testing* than TM and that Chatbot+PN will lead to a higher *Testing* than Chatbot without PN. These hypotheses will be tested at alpha of .05.

Secondary and Implementation Outcomes. We will evaluate Chatbot+PN versus Chatbot, interaction effects, and indicators of TM, Chatbot, and PN implementation among participants. Implementation outcomes measure the extent of the delivery and adaptation of intervention components, including *Reach-Engage Testing* (proportion of participants who are offered at-home testing and reply to the message or launch the Chatbot), *Reach-Accept Testing* (proportion of participants who are offered at-

home testing and reply accepting or select "Send me a test" on the Chatbot), *PN-Request* (proportion of participants in the PN condition who request patient navigation), *PN-Engage* (proportion of participants in the PN condition who talk to a patient navigator), and *Opt-Out* (proportion of participants who opt-out). We will analyze chatbot usage patterns (e.g., time using chatbot, topics visited) as listed in Table 1.

Predictors and Moderators of Study Outcomes. We will assess predictors and moderators including demographics, vaccination status, and Tier 1 Common Data Elements (CDEs) used by the Rapid Acceleration of Diagnostics-Underserved Populations (RADx-UP) program of the U.S. National Institutes of Health (NIH).[56]

Study Assessments. The primary outcome *Testing* will be collected through two methods from patients who requested a test kit: (i) a brief text message sent 90 days after the first exposure to interventions asking if they used the mailed COVID-19 test (patients are asked to reply with a single YES or NO response to the text message); and (ii) a survey sent to participants 7 days after the last exposure to study interventions (Day 97). Secondary outcomes *Reach-Engage Testing, Reach-Accept Testing, PN-Request*, *PN-Engage,* and *Opt-Out* will be obtained from computer system logs. The survey will also collect Tier 1 CDEs. To complete the survey, participants will be invited via mail and text message to complete a survey. Non-responders will also be called via phone to complete an interviewer-administered survey. Vaccination status will be obtained from the Utah State Immunization Information System (USIIS). Other predictors and moderators of study outcomes will be collected from EHR data (e.g., demographics) and online surveys (i.e., Tier 1 CDEs).

Table 1 - Study Assessments.

Assessment	Baseline	During exposure to interventions	Day 90 Follow-Up (via text msg)	Day 97 Follow-Up (via survey)	Description
Demographics	X			X	Age sex, race, ethnicity, preferred language, insurance status, etc.
Testing (primary outcome)			X	X	Proportion of study

Assessment	Baseline	During exposure to interventions	Day 90 Follow-Up (via text msg)	Day 97 Follow-Up (via survey)	Description
					participants who use an at-home COVID-19 test during the course of the study
Number of tests used			X	X	Self-reported number of tests used by each study participant who requested a test.
Vaccination status	X			X	COVID-19 vaccination status according to state immunization registry
NIH RADx-UP CDE data elements (Tier 1)				X	Comprehensive questionnaire (234 items) including demographics, COVID testing, symptoms, health status, social determinants of health, etc.
Implementation Outcomes					
Reach-Engage Testing		X			Proportion of participants who are offered at-home testing and reply to the message or launch the chatbot
Reach-Engage Frequency		X			Number of times a participant replied to a message offering at-home testing or launched the chatbot
Reach-Accept Testing		X			Proportion of participants who are offered at-home testing and reply accepting
Reach-Engage Frequency		X			Number of times a participant replied to a message/chatbot requesting at-home testing
PN-Request		X			Proportion of participants in the PN condition who request patient navigation
PN-Request Frequency		X			Number of times a participant requested to speak with a patient navigator

Assessment	Baseline	During exposure to interventions	Day 90 Follow-Up (via text msg)	Day 97 Follow-Up (via survey)	Description
PN-Engage		X			Proportion of participants in the PN condition who talk to a patient navigator
PN-Engage Frequency		X			Number of times a participant spoke with a patient navigator
Opt-Out		X			Proportion of participants who opted-out
Chatbot use					
Chatbot session length		X			Amount of time spent using the chatbot in a session
Chatbot timeout		X			Proportion of chatbot sessions that timed out without reaching an endpoint (e.g., close chatbot window, request test, request to talk to patient navigator)
Chatbot actions		X			Number of chatbot topics clicked per session
Chatbot test request only		X			Proportion of chatbot session in which the only action was requesting a test
Chatbot coverage		X			Proportion of chatbot contents that are accessed per session
Chatbot topics		X			Proportion of sessions in which a specific chatbot topic is accessed

Statistical Analysis. The main effects of each intervention will be evaluated using a logistic regression model by regressing 90-day testing upon each of the three main effects: Chatbot (vs. TM) with an indicator for self-reporting to have a smartphone, PN (vs. no PN), and outreach frequency (10 vs. 30 days). We will preliminarily include the pairwise interactions of the main effects, and the three-way interaction to assess for any synergistic and/or antagonistic effect modifications across interventions and will include any statistically significant effect modifications (i.e., interactions) in the primary analysis

model. The model will adjust for whether the patient self-reported having a smartphone. Estimates and 95% confidence intervals will be reported for each main effect and interaction effect. If an interaction term was included for having evidence of an effect modification, we will report the main effects separately for each level of the effect modifying intervention. The model will be run on all participants to evaluate the primary hypotheses, each tested at alpha of .0167, and it will be applied to the smartphone participants to evaluate the secondary hypotheses.

Among the smartphone subgroup, we will fit the primary analysis model to evaluate all other main effects as a secondary analysis. We will also test the added effect of PN among those randomized to receive Chatbot. Among the remaining patients, we will regress 90-day testing upon PN (yes vs no) and outreach frequency (10 vs 30 days). We will include an interaction if a preliminary model provides evidence of an effect modification. Side-by-side, we will present the estimated effects across all patients and by smartphone ownership subgroup.

Handling Missing Data. The primary analysis will assume missing outcomes and covariates are missing at random (MAR). Under this assumption, observed covariates can be used to explain the missingness mechanism. When conditioning on observed covariates, the distribution of outcomes is assumed to be similar among responders and non-responders. With this framework, we will omit missing outcomes,[57] multiply impute missing covariates using a fully conditional specified model,[58] and account for the multiple imputations in analysis.[59] While MAR is considered a reasonable starting point assumption for missing data, it is plausible that responders and non-responders have different outcomes beyond what can be adjusted by covariates (i.e., missing not at random; MNAR). We will use pattern mixture models as a sensitivity analysis to assess the robustness of conclusions under the MAR assumption.[60]

Sample Size Justification. Power for SCALE-UP II was evaluated for a target enrollment of 42,000 adults aged 18 year and older who receive care at the three participating CHCs, have a valid cellphone recorded in the EHR, and have English or Spanish as their preferred language in the EHR. Among those patients, we anticipate fewer than 10% opt outs. We assume 75% will have a smartphone

and 10% to self-report as having a smartphone. Among these patients with a self-reported smartphone, we anticipate ~375 patients in each of the eight study arms. Among patients who do not self-report as having a smartphone, we expect ~8,750 patients in each of the four arms.

We hypothesize that TM with no PN and a 30-day outreach will have a 5% at-home testing rate and that PN, Chatbot, and 10-day outreach frequency will increase the testing rate by 5% each without a synergistic effect. We hypothesize the at-home testing rate to be 5% less when outreach occurs every 30 days. We anticipate a ≥ 40% response rate for the primary outcome. Under these assumptions, and with alpha adjusted to .0167, we are essentially fully powered to test the primary hypotheses. If the response rate is 20%, we are at least 85% powered to test these effects. In secondary analyses, with alpha of .05 and a 40% response rate, we are 75% powered to detect the Chatbot main effect of and 68% powered to detect the added effect of PN.

DISCUSSION

Individuals from historically marginalized communities have suffered substantial health inequities throughout the COVID-19 pandemic, not only in terms of outcomes but also vaccination rates and access to testing.[1-8,61,62] PHM approaches leveraging widely adopted EHR systems and technology such as cellphones provide excellent opportunities to deliver scalable interventions to improve health equity. The SCALE-UP II trial aims to examine scalable and sustainable PHM interventions to increase the uptake of at-home COVID-19 testing among individuals who receive care from low resource CHCs. Strengths include a pragmatic trial with broad inclusion criteria leveraging existing EHR data; highly scalable automated interventions; and a novel design that compares two digital patient engagement approaches (TM and Chatbot), examines the added effect of a human-augmented intervention (patient navigation) over digital interventions, and compares two frequencies (every 10 days or 30 days) of repeated offers to receive COVID-19 testing.

Even though public health agencies worldwide have declared the end of the COVID-19 pandemic, COVID-19 testing is still critical to help reduce exposure and to identify individuals who can benefit from treatment. In addition, approaches are needed to support public health preparedness for

future pandemics and outbreaks. The proposed interventions in SCALE-UP II leverage resources that are currently available at CHCs and therefore can be sustained in the long term.

Limitations

The study design has several limitations. First, a potentially low response rate to the introductory message asking about smartphone ownership could lead to a small sample size and randomization of only motivated individuals to the chatbot condition. We considered randomizing all participants to Chatbot vs. TM, but patients who do not have a smartphone (estimated as 25% of the CHC patient population) and are randomized to the chatbot condition would not be able to use the chatbot, compromising study reach. Second, the study relies on self-report for the primary outcome (*Testing*). To maximize response rates, we use two approaches to collect the primary outcome: a quick question via text messaging after exposure to study interventions and a survey at the end of the study. Last, the study will be conducted after the peak of the pandemic, when participants may be less motivated to learn about and receive COVID-19 testing. Also, individuals have been overexposed to information about COVID-19 from multiple sources and may have already formed their opinions about COVID-19 and COVID-19 testing. Therefore, it is possible that study findings may not generalize to the context of new onset of a pandemic or outbreak.

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Competing interests statement. The authors declare no competing interests.

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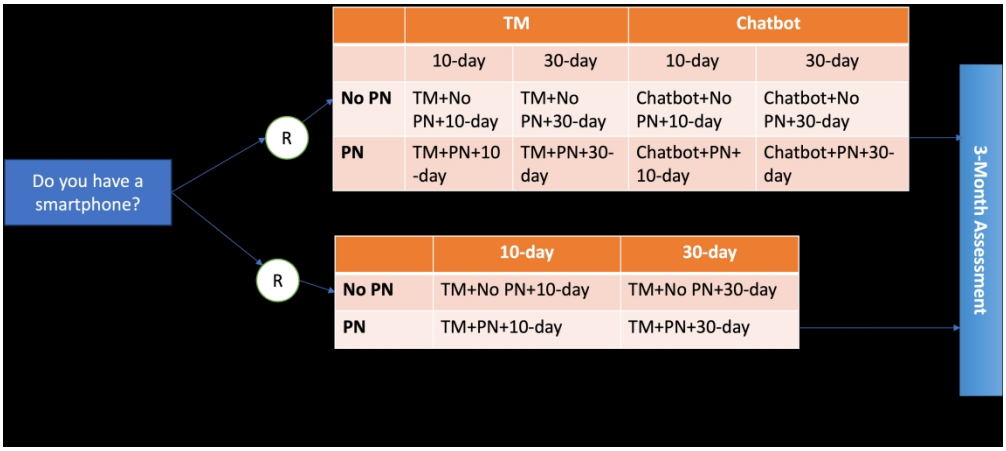

Figure 1 – SCALE-UP II Trial Design

327x144mm (300 x 300 DPI)

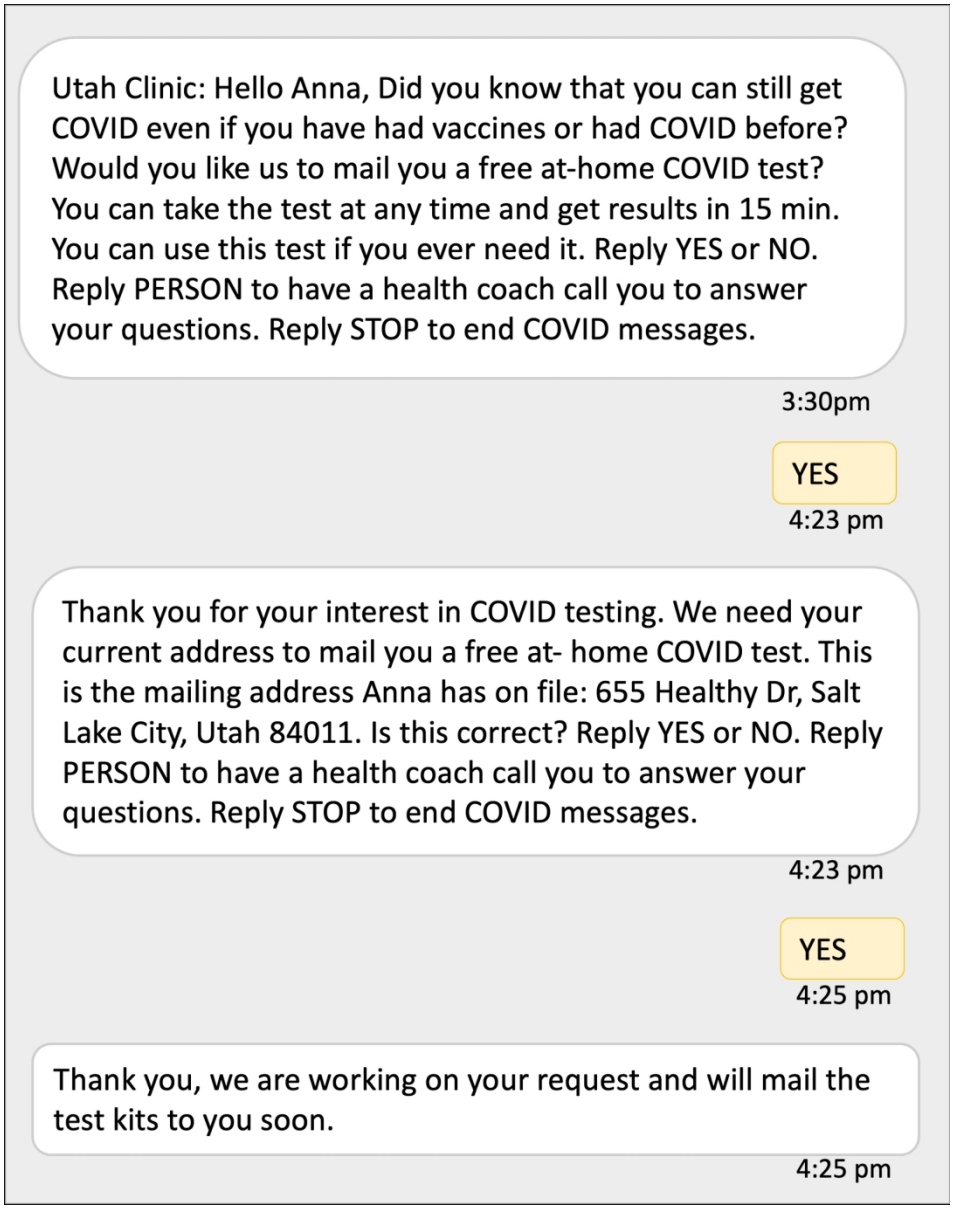

Figure 2 – Sample text message conversation offering COVID-19 at-home testing.

149x188mm (300 x 300 DPI)

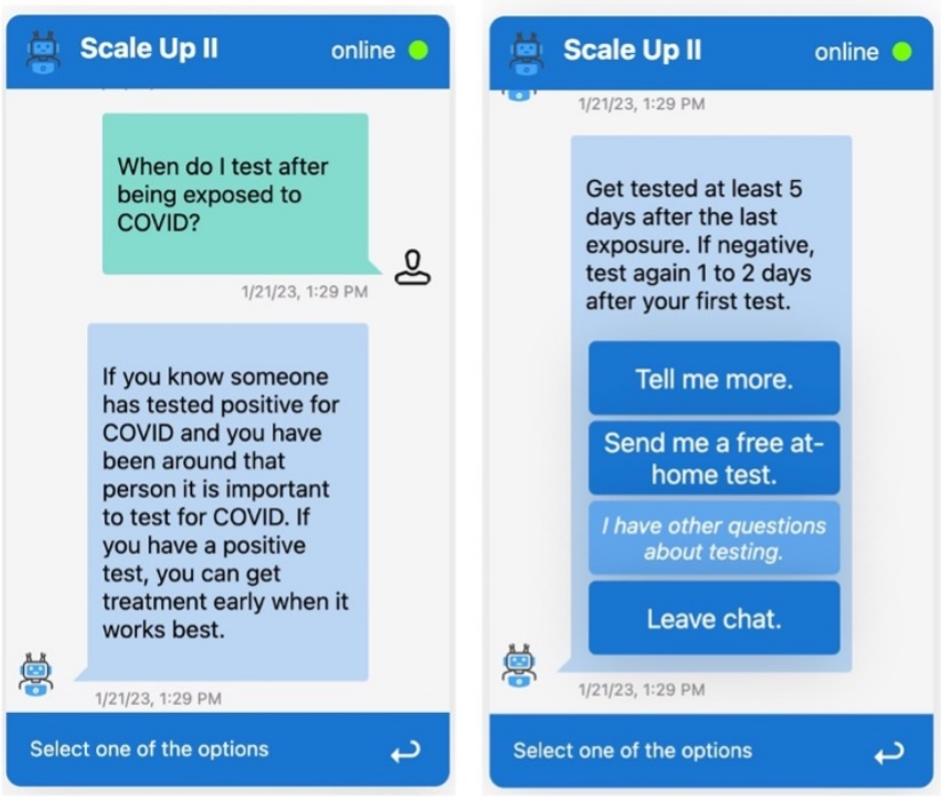

Figure 3 – Sequential screenshot of chatbot intervention showing a question being answered, followed by options to ask further questions, and request a COVID-19 test kit to be mailed to the patient's home.

101x81mm (220 x 220 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	18
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	18
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4 and 5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	5-7
Objectives	#7	Specific objectives or hypotheses	12
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will	7

		perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-11
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	NA
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	NA
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-15
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11-12
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7-8

Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7-8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7-8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7-8
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-15
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13-15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13-15
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	12-17
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12-17

Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	NA
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	5
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	5
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7

Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	18
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	2
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	NA
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

BMJ Open

SCALE-UP II: Protocol for a Pragmatic Randomized Trial Examining Population Health Management Interventions to Increase the Uptake of At-Home COVID-19 Testing in Community Health Centers

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SCALE-UP II: Protocol for a Pragmatic Randomized Trial Examining Population Health Management Interventions to Increase the Uptake of At-Home COVID-19 Testing in Community Health Centers

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ABSTRACT

Introduction. SCALE-UP II aims to investigate the effectiveness of population health management interventions using text messaging (TM), chatbots, and patient navigation (PN) in increasing the uptake of at-home COVID-19 testing among patients in historically marginalized communities, specifically those receiving care at community health centers (CHCs).

Methods and Analysis. The trial is a multi-site, randomized pragmatic clinical trial. Eligible patients are ≥ 18 years old with a primary care visit in the last three years at one of the participating CHCs. Demographic data will be obtained from CHC electronic health records. Patients will be randomized to one of two factorial designs based on smartphone ownership. Patients who self-report replying to a text message that they have a smartphone will be randomized in a 2x2x2 factorial fashion to receive (i) chatbot or TM; (ii) PN (yes or no); and (iii) repeated offers to interact with the interventions every 10 or 30 days. Participants who do not self-report as having a smartphone will be randomized in a 2x2 factorial fashion to receive (i) TM with or without PN; and (ii) repeated offers every 10 or 30 days. The interventions will be sent in English or Spanish, with an option to request at-home COVID-19 test kits. The primary outcome is the proportion of participants using at-home COVID-19 tests during a 90-day follow-up. The study will evaluate main effects and interactions among interventions, implementation outcomes, and predictors and moderators of study outcomes. Statistical analyses will include logistic regression, stratified subgroup analyses, and adjustment for stratification factors.

Ethics and dissemination: The protocol was approved by the University of Utah Institutional Review Board. On completion, study data will be made available in compliance with National Institutes of Health data sharing policies. Results will be disseminated through study partners and peer-reviewed publications.

Trial registration: Clinicaltrials.gov (NCT05533918 and NCT05533359).

Keywords: COVID-19, digital health, health equity, population health management

Strengths and limitations of this study

Strengths

- Uses scalable population health management interventions to increase the reach and uptake of at-home COVID-19 testing.
- Dissemination strategy modalities (i.e., voice and text cellphones) are nearly ubiquitous among adults in the United States, including among historically marginalized populations.

Limitations

- The study relies on self-reported data for its primary outcome (use of at-home testing).
- Patient population will be drawn from community health centers that opted to participate in this study, all of which are located in a single state in the United States, which limits generalizability.

INTRODUCTION

Racial/ethnic minority, low socioeconomic status (SES), and rural populations suffer profound health inequities across a wide variety of conditions, including a higher rate of hospitalization and mortality due to COVID-19.[1-4] Similar inequities have been found across the US for vaccination rates between urban and rural,[5] high and low SES,[6] and White and non-White populations.[7, 8] Low vaccination rates and withdrawal of protection measures leave historically marginalized populations at high risk for local outbreaks and more contagious variants.

Although public health agencies worldwide have declared the end of the pandemic, timely testing is still important to help reduce exposure and offer timely treatment to individuals at a higher risk for severe disease. However, historically marginalized communities lacked easy and convenient access to testing throughout the COVID-19 pandemic, especially after the closure of mass test sites nationwide.[9, 10] Although several FDA-approved at-home tests are available, providing a convenient, quick and low-cost alternative for patients to test at home,[11, 12] substantial disparities exist in the use of at-home COVID-19 testing. While the use of at-home COVID-19 testing has more than tripled between the Delta and Omicron outbreaks, use of at-home testing was more than twice as high among individuals identifying as White, having high SES, and having a postgraduate degree.[13] Thus, scalable approaches are needed to promote the uptake of at-home COVID-19 testing among individuals from historically marginalized communities.

Despite evidence of a digital divide between high resource healthcare systems and low resource community health centers (CHCs),[14, 15] historically marginalized populations have almost universal access to technology such as cellphones, which provide opportunities for large scale population health management (PHM) interventions. Even in households with annual incomes less than $30,000, 97% own a cellphone and 76% own a smartphone.[16] The SCALE-UP II trial will investigate three PHM interventions (text messaging [TM], automated chatbot, and patient navigation [PN]) to increase the reach and uptake of at-home COVID-19 testing among patients who receive care at CHCs.

METHODS AND ANALYSIS

This protocol was developed using the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT).[17] The protocol was approved by the Institutional Review Board at the University of Utah on June 10, 2022 (IRB_00150669). The trial was registered with Clinicaltrials.gov (NCT05533359 for patients self-reporting that they have a smartphone and NCT05533918 for all other patients) on September 9, 2022. Enrollment was planned to begin in December 2022 and data collection was planned to end in November 2023.

Patient and Public Involvement

SCALE-UP II is conducted in partnership with the Association for Utah Community Health (AUCH), CHCs across Utah, the Utah Department of Health and Human Services (UDHHS), and the University of Utah. Our research-practice partnership uses a multi-pronged community engagement approach to (i) identify research questions, (ii) develop, adapt, and implement interventions, and (iii) inform dissemination plans.[18, 19] The community engagement approach includes a weekly project meeting with AUCH, UDHHS, and the research team and quarterly Patient Advisory Committee (PAC; consisting of CHC patient representatives) and Study Advisory Committee (SAC; consisting of patients, CHC staff, UDHHS, and AUCH representatives) meetings. The research objectives of SCALE-UP II were identified in partnership with AUCH and UDHHS; both AUCH and UDHHS were interested in addressing the impact of COVID-19 among historically marginalized communities in Utah. Input from the PAC informed the design of the text messaging and chatbot interventions. Furthermore, TM and Chatbot scripts were developed following information gathered from community members in Utah.

Study Design

SCALE-UP II is an individually randomized, multi-site, pragmatic clinical trial. The experimental design varies according to each patient's response to a text message asking if they have a smartphone. Participants who self-report that they have a smartphone will be randomized in a 2x2x2 factorial fashion to receive (i) chatbot or TM; (ii) PN (yes or no); and (iii) repeated offers to interact with the interventions every 10 or 30 days. Participants who do not respond to the introductory text message or who self-report

as not having a smartphone will be randomized in a 2x2 factorial fashion to receive (i) TM with or without PN; and (ii) repeated offers every 10 or 30 days.

Figure 1 – SCALE-UP II Trial Design.

Rationale for Study Design

The interventions in SCALE-UP II interventions leverage (i) wide adoption of electronic health record (EHR) systems, even in low resource CHCs;[20, 21] (ii) wide adoption of cellphones with at least voice and text capabilities;[16] and (iii) the low cost, efficiency, and simplicity of at-home COVID-19 tests.[11, 12] Therefore, SCALE-UP II is designed to maximize reach with low-cost interventions to increase the uptake of COVID-19 testing in historically marginalized communities.

SCALE-UP II will enroll patients from Utah CHCs. These settings provide primary care to diverse, low SES populations, and provide an ideal setting to address COVID-19 because there is an established relationship and coordination of care, and ~80% of individuals see a primary care provider at least annually.[22] Three Utah CHC systems and their 12 primary care clinics will participate in SCALE-UP II. Demographics of SCALE-UP II CHC patients include: 51% Latino, 62% ≤100% federal poverty level, 69% uninsured, and receiving care in clinics where 17% are in rural/frontier areas.[23]

Since the chatbot requires a smartphone with connection to the internet, and about 25% of individuals with low SES and from rural areas do not have a smartphone,[16] SCALE-UP II will enroll patients in one of two factorial designs based on their smartphone ownership in order to maximize reach to the 96% of individuals who own at least a voice and text cellphone.

Patients may be reluctant to test due to hesitancy and numerous other barriers.[24, 25] However, practical advice from patient navigators such as community health workers can help overcome hesitancy and engagement barriers such as logistics, transportation, and expense; of critical importance, providers welcome the use of these approaches with their patients.[26-28] Thus, in addition to the TM and chatbot interventions, SCALE-UP II will examine the added effect of offering access to patient navigation upon request through either intervention. Since patient navigation is a human-intensive intervention, examining

the uptake of patient navigation when provided only upon request is critical for conserving resources in limited resource settings such as CHCs.

Participants

The study inclusion criteria aim to enroll a broad range of individuals to maximize reach. Eligible patients will be those who (i) have been seen at one of the participating CHCs in the last three years, (ii) are 18 years and older, (iii) have a working cellphone listed in the CHC EHR, and (iv) indicate a language preference in the EHR of English or Spanish.

The study will exclude participants who opt out upon receipt of the introductory message asking about smartphone ownership. Also, if more than one patient shares the same smartphone number in the EHR, only the patient with the most recent documented clinical encounter will be included.

Recruitment

As a pragmatic trial with interventions that offer minimal risk, the University of Utah IRB approved a waiver of consent for randomization and receipt of PHM interventions. Therefore, all participants who meet eligibility criteria will be automatically enrolled in the study. All three study points of contact (TM, chatbot, PN) will allow participants to opt-out through a simple reply at any time. Participants will be consented to complete the 3-month follow-up survey prior to survey completion using a consent cover letter.

Randomization and Blinding

Participants who self-report having a smartphone will be randomized to one of eight study arms (Figure 1): (1) TM+10-day, (2) TM+30-day, (3) Chatbot+10-day, (4) Chatbot+30-day, (5) TM+PN+10-day, (6) TM+PN+30-day, (7) Chatbot+PN+10-day, or (8) Chatbot+PN+30-day. Participants who do not self-report to have a smartphone will be randomized to one of four study arms: (1) TM+10-day, (2) TM+30-day, (3) TM+PN+10-day, or (4) TM+PN+30-day. Participants will be randomized after receiving the introductory text message asking if they have access to a smartphone.

Randomization will be implemented by software and will utilize randomized permuted blocks to guard against any biases due to ordering of patients. Furthermore, the randomization will be stratified by

CHC and urban/rural designation of the participant's zip code according to rural-urban commuting area (RUCA) codes.

The study is outcome assessor and investigator blinded. Patient navigators cannot be blinded to treatment assignment. Participants will be blinded to study participation.

Study Interventions

Overall, all study interventions (i) are sent on behalf of the participant's clinic, (ii) offer the option to request at-home mailed COVID-19 test kits at no cost for use as needed, (iii) are provided automatically in English or Spanish based on the patient's preferred language in the CHC EHR, and (iv) provide an option for participants to opt-out at any time (see Figures 2 and 3). Eligible patients and their demographics data (e.g, name, date of birth, race, ethnicity, language, address, cellphone) will be extracted from the CHC EHRs through EHR reports prior to the trial launch. Demographics data will be used to determine eligibility, support study interventions, and for study analyses.

Figure 2 – Sample text message conversation offering COVID-19 at-home testing.

Figure 3 – Sequential screenshot of chatbot intervention showing a question being answered, followed by options to ask further questions, and request a COVID-19 test kit to be mailed to the patient's home.

Text Messaging (TM). Meta-analyses of text messaging interventions have found these approaches to be promising for improving compliance with healthy behaviors and preventive care, beneficial for multiple racial/ethnic groups, and inexpensive to deliver.[29-34] A US Department of Health and Human Services review concluded: *With the near-ubiquitous presence of cellphones and the rapid growth of smartphones, text messaging and other mHealth interventions can remove traditional geographic and economic barriers to access to health information and services. The higher rates of mobile phone ownership and use among Blacks and Hispanics, compared to Whites, are particularly noteworthy. These interventions have the potential to improve health knowledge, behaviors, and outcomes and, ultimately, to reduce disparities*.[34] Our own research has demonstrated that a simple, repeated

offer to connect unmotivated, low-SES individuals with treatment resources resulted in 25% of individuals enrolling in tobacco cessation treatment.[35] Thus, repeated prompting offering access to COVID-19 testing via texts is an extremely convenient, low cost, scalable approach for increasing testing uptake.

TM will consist of bidirectional text messaging sent on behalf of the participant's clinic with a response option for patients to request at-home mailed COVID-19 test kits at no cost (Figure 2). Participants randomized to TM+PN will also be able to reply requesting to speak with a patient navigator. Messages will be sent in English or Spanish based on the patient's language preference in the EHR.

Chatbot. Chatbots are automated conversational agents designed to mimic human interaction. Chatbots are increasingly popular in various health contexts as they can be easily accessed through smartphones, tablets, laptops, or desktops. Chatbots have many advantages for patient engagement, including providing scripted education interactively, chunking information into small segments that are easier to process, and allowing for choice in the amount of information received. Chatbots are accessible to the vast majority of U.S. adults. Even in households with annual incomes less than $30,000, 76% own a smartphone.[16, 36, 37] Delivery of health services through chatbots in research contexts has been successfully tested in various health domains such as mental health, asthma, diabetes management, and physical activity uptake.[38] While scripted chatbots have been widely used in the COVID-19 pandemic, especially to evaluate patient's eligibility for testing and vaccination,[39-44] research is needed to examine their benefits in addressing COVID-19 at-home testing. In addition, there is a lack of studies that investigated the design and implementation of chatbots specifically for historically marginalized populations.

For SCALE-UP II, we designed a scripted chatbot (i.e., predefined conversation script, and a fixed set of questions and scripted answers) that presents participants with a list of topics that address most common knowledge gaps and hesitancy factors related to at-home COVID-19 testing (Figure 3). The chatbot script was designed and guided by findings from a national survey and in-depth interviews with participants in the targeted Utah population, both conducted by our team. The following topics are

covered: benefits of testing (even when already vaccinated or previously had COVID), when to test, test accuracy, how to use a test, and what to do if a test is positive. Both text messaging and chatbot scripts were validated through feedback from the study and patient advisory committee composed of clinical staff and patients from the participating CHCs.

Patients in the chatbot condition will receive a text message on behalf of their clinic offering a hyperlink to access the chatbot on the phone's web browser. At any point in the chatbot, participants will be able to click a button to request an at-home test kit. Participants randomized to the PN condition can also click PERSON to request to speak to a patient navigator. As in TM, the chatbot is offered both in English and Spanish.

Patient Navigation (PN). SCALE-UP II will use community health workers (CHWs) employed by AUCH as patient navigators to address practical barriers, motivation, and hesitancy to COVID-19 testing. To assist navigators in working with patients, CHWs will be trained in an empirically-validated behavior change approach (Motivation And Problem Solving; MAPS).[45-50] MAPS is a holistic, dynamic approach to behavior change that integrates two empirically validated approaches (motivational interviewing[51, 52] and practical problem solving[47, 53, 54]) for helping patients engage in target behaviors.[45-47, 49, 50] Importantly, MAPS addresses patients' social determinants of health, and provides practical advice and connections to services whenever possible, including addressing testing concerns (e.g., worries about repercussions of a positive test, infecting family members, quarantining, financial). MAPS has been demonstrated to be effective in numerous randomized controlled trials with respect to increasing enrollment in evidence-based interventions, as well as enhancing and maintaining behavior change.[45-47, 49, 50]

All SCALE-UP II navigators will receive ~20 hours of training, consistent with recommended training for helpline specialists.[55] Participants randomized to the PN condition who request to speak with a patient navigator will receive a phone call within 48 hours, although it is anticipated that most patients would be called within the same day or in the next day. Patient navigators will make three attempts to contact a participant.

Study Roll-Out Schedule

To ensure that the interventions work properly with real patient data, a pilot study will be conducted with a random sample of patients from one of the participating CHCs both for the TM and Chatbot interventions.

For the remainder of patients, to address bottlenecks that depend on non-automated processes (e.g., mailing of test kits, patient navigation), study participants will be exposed to interventions in one of 14 weekly batches according to a pre-defined schedule, in which a cohort with a new set of participants is added to the study every week. Participants will be randomly allocated across the 14 batches, also stratified by CHC and urban vs. rural.

Every cycle starts by sending the introductory message to participants in the cohort (Day -2). Participants will have two days to respond. After that, eligible participants will be randomized into one of the two factorial designs depending on their response to the introductory message (Day 0). After randomization, participants will receive messages offering access to at-home testing once every 10 versus 30 days for 7 weeks (Days 0, 10, 20, 30, 40, 50, and 60 vs. Days 0, 30, and 60).

Outcome Assessment

The main study outcomes are described below. Table 1 provides a complete list including the primary, secondary outcomes, and implementation outcomes, as well as predictors and moderators of study outcomes.

Primary Outcomes and Hypotheses. The primary outcome is *Testing*; the proportion of study participants who use an at-home COVID-19 test at least once during the course of 90-day study follow-up as defined below. For all patients, regardless of self-report of smartphone ownership, the primary hypotheses are main effects for PN (PN > No PN), main effects for message frequency (10-day > 30-day), and that TM+PN will lead to higher *Testing* than TM. These hypotheses will be tested at an alpha of .0167, adjusted for multiple comparisons using the Bonferroni method. Because we anticipate a low sample size of smartphone self-reporters to be adequately powered, we consider Chatbot-related

hypotheses as secondary. These include the hypothesis that Chatbot will lead to a higher *Testing* than TM and that Chatbot+PN will lead to a higher *Testing* than Chatbot without PN. These hypotheses will be tested at alpha of .05.

Secondary and Implementation Outcomes. We will evaluate Chatbot+PN versus Chatbot, interaction effects, and indicators of TM, Chatbot, and PN implementation among participants. Implementation outcomes measure the extent of the delivery and adaptation of intervention components, including *Reach-Engage Testing* (proportion of participants who are offered at-home testing and reply to the message or launch the Chatbot), *Reach-Accept Testing* (proportion of participants who are offered at-home testing and reply accepting or select "Send me a test" on the Chatbot), *PN-Request* (proportion of participants in the PN condition who request patient navigation), *PN-Engage* (proportion of participants in the PN condition who talk to a patient navigator), and *Opt-Out* (proportion of participants who opt-out). We will analyze chatbot usage patterns (e.g., time using chatbot, topics visited) as listed in Table 1.

Predictors and Moderators of Study Outcomes. We will assess predictors and moderators including demographics, vaccination status, and Tier 1 Common Data Elements (CDEs) used by the Rapid Acceleration of Diagnostics-Underserved Populations (RADx-UP) program of the U.S. National Institutes of Health (NIH).[56]

Study Assessments. The primary outcome *Testing* will be collected through two methods from patients who requested a test kit: (i) a brief text message sent 90 days after the first exposure to interventions asking if they used the mailed COVID-19 test at least once (patients are asked to reply with a single YES or NO response to the text message); and (ii) a survey sent to participants 7 days after the last exposure to study interventions (Day 97). Secondary outcomes *Reach-Engage Testing, Reach-Accept Testing, PN-Request*, *PN-Engage,* and *Opt-Out* will be obtained from computer system logs. The survey will also collect Tier 1 CDEs. To complete the survey, participants will be invited via mail and text message to complete a survey. Non-responders will also be called via phone to complete an interviewer-administered survey. Vaccination status will be obtained from the Utah State Immunization Information System (USIIS). Other predictors and moderators of study outcomes will be collected from EHR data

(e.g., demographics) and online surveys (i.e., Tier 1 CDEs).

Table 1 - Study Assessments.

Assessment	Baseline	During exposure to interventions	Day 90 Follow-Up (via text msg)	Day 97 Follow-Up (via survey)	Description
Demographics	X			X	Age sex, race, ethnicity, preferred language, insurance status, etc.
Testing (primary outcome)			X	X	Proportion of study participants who use an at-home COVID-19 test during the course of the study
Number of tests used			X	X	Self-reported number of tests used by each study participant who requested a test.
Vaccination status	X			X	COVID-19 vaccination status according to state immunization registry
NIH RADx-UP CDE data elements (Tier 1)				X	Comprehensive questionnaire (234 items) including demographics, COVID testing, symptoms, health status, social determinants of health, etc.
Implementation Outcomes					
Reach-Engage Testing		X			Proportion of participants who are offered at-home testing and reply to the message or launch the chatbot
Reach-Engage Frequency		X			Number of times a participant replied to a message offering at-home testing or launched the chatbot
Reach-Accept Testing		X			Proportion of participants who are offered at-home testing and reply accepting
Reach-Engage Frequency		X			Number of times a participant replied to a

Assessment	Baseline	During exposure to interventions	Day 90 Follow-Up (via text msg)	Day 97 Follow-Up (via survey)	Description
					message/chatbot requesting at-home testing
PN-Request		X			Proportion of participants in the PN condition who request patient navigation
PN-Request Frequency		X			Number of times a participant requested to speak with a patient navigator
PN-Engage		X			Proportion of participants in the PN condition who talk to a patient navigator
PN-Engage Frequency		X			Number of times a participant spoke with a patient navigator
Opt-Out		X			Proportion of participants who opted-out
Chatbot use					
Chatbot session length		X			Amount of time spent using the chatbot in a session
Chatbot timeout		X			Proportion of chatbot sessions that timed out without reaching an endpoint (e.g., close chatbot window, request test, request to talk to patient navigator)
Chatbot actions		X			Number of chatbot topics clicked per session
Chatbot test request only		X			Proportion of chatbot session in which the only action was requesting a test
Chatbot coverage		X			Proportion of chatbot contents that are accessed per session
Chatbot topics		X			Proportion of sessions in which a specific chatbot topic is accessed

Statistical Analysis. The main effects of each intervention will be evaluated using a logistic regression model by regressing 90-day testing upon each of the three main effects: Chatbot (vs. TM) with an indicator for self-reporting to have a smartphone, PN (vs. no PN), and outreach frequency (10 vs. 30 days). We will preliminarily include the pairwise interactions of the main effects, and the three-way interaction to assess for any synergistic and/or antagonistic effect modifications across interventions and will include any statistically significant effect modifications (i.e., interactions) in the primary analysis model. The model will adjust for whether the patient self-reported having a smartphone. Estimates and 95% confidence intervals will be reported for each main effect and interaction effect. If an interaction term was included for having evidence of an effect modification, we will report the main effects separately for each level of the effect modifying intervention. The model will be run on all participants to evaluate the primary hypotheses, each tested at alpha of .0167, and it will be applied to the smartphone participants to evaluate the secondary hypotheses.

Among the smartphone subgroup, we will fit the primary analysis model to evaluate all other main effects as a secondary analysis. We will also test the added effect of PN among those randomized to receive Chatbot. Among the remaining patients, we will regress 90-day testing upon PN (yes vs no) and outreach frequency (10 vs 30 days). We will include an interaction if a preliminary model provides evidence of an effect modification. Side-by-side, we will present the estimated effects across all patients and by smartphone ownership subgroup.

Handling Missing Data. The primary analysis will assume missing outcomes and covariates are missing at random (MAR). Under this assumption, observed covariates can be used to explain the missingness mechanism. When conditioning on observed covariates, the distribution of outcomes is assumed to be similar among responders and non-responders. With this framework, we will omit missing outcomes,[57] multiply impute missing covariates using a fully conditional specified model,[58] and account for the multiple imputations in analysis.[59] While MAR is considered a reasonable starting point assumption for missing data, it is plausible that responders and non-responders have different outcomes beyond what can be adjusted by covariates (i.e., missing not at random; MNAR). We will use pattern

mixture models as a sensitivity analysis to assess the robustness of conclusions under the MAR assumption.[60]

Sample Size Justification. Power for SCALE-UP II was evaluated for a target enrollment of 42,000 adults aged 18 year and older who receive care at the three participating CHCs, have a valid cellphone recorded in the EHR, and have English or Spanish as their preferred language in the EHR. This estimate is based on the patient population that has received care at the three participating CHC within in the 3 years preceding the trial and who meet the inclusion criteria. Among those patients, we anticipate fewer than 10% opt outs based on prior studies using similar population health management approaches with the same CHCs.[61] Based on national estimates of smartphone ownership,[62] we assume 75% will have a smartphone and 10% to self-report as having a smartphone. Among these patients with a self-reported smartphone, we anticipate ~375 patients in each of the eight study arms. Among patients who do not self-report as having a smartphone, we expect ~8,750 patients in each of the four arms.

Based on results of our previous trial using text messaging to help patients with access to COVID-19 testing,[61] we estimate that TM with no PN and a 30-day outreach will have a 5% at-home testing rate and that PN, Chatbot, and 10-day outreach frequency will increase the testing rate by 5% each without a synergistic effect. We hypothesize the at-home testing rate to be 5% less when outreach occurs every 30 days. Based on a similar trial conducted with patients from the same CHCs, we anticipate a $\geq$ 40% response rate for the primary outcome.[63] Under these assumptions, with alpha adjusted to .0167, and assuming the response rate is 20%, we are at least 85% powered to test these effects. In secondary analyses, with alpha of .05 and a 40% response rate, we are 75% powered to detect the Chatbot main effect of and 68% powered to detect the added effect of PN.

Ethics and dissemination

All procedures performed in studies involving human participants will be conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The protocol for this study was approved by the University of Utah Institutional Review Board (00150669). Materials used to conduct the

study are not currently publicly available. Materials may be requested by emailing the corresponding author. Study results will be disseminated via peer-reviewed publications and manuscripts, as well as to the health system and community partners via lay reports and presentations.

DISCUSSION

Individuals from historically marginalized communities have suffered substantial health inequities throughout the COVID-19 pandemic, not only in terms of outcomes but also vaccination rates and access to testing.[1-8, 64, 65] PHM approaches leveraging widely adopted EHR systems and technology such as cellphones provide excellent opportunities to deliver scalable interventions to improve health equity. The SCALE-UP II trial aims to examine scalable and sustainable PHM interventions to increase the uptake of at-home COVID-19 testing among individuals who receive care from low resource CHCs. Strengths include a pragmatic trial with broad inclusion criteria leveraging existing EHR data; highly scalable automated interventions; and a novel design that compares two digital patient engagement approaches (TM and Chatbot), examines the added effect of a human-augmented intervention (patient navigation) over digital interventions, and compares two frequencies (every 10 days or 30 days) of repeated offers to receive COVID-19 testing.

Even though public health agencies worldwide have declared the end of the COVID-19 pandemic, COVID-19 testing is still critical to help reduce exposure and to identify individuals who can benefit from treatment. In addition, approaches are needed to support public health preparedness for future pandemics and outbreaks. The proposed interventions in SCALE-UP II leverage resources that are currently available at CHCs and therefore can be sustained in the long term.

Limitations

The study design has several limitations. First, a potentially low response rate to the introductory message asking about smartphone ownership could lead to a small sample size and randomization of only motivated individuals to the chatbot condition. We considered randomizing all participants to Chatbot vs. TM, but patients who do not have a smartphone (estimated as 25% of the CHC patient population) and are randomized to the chatbot condition would not be able to use the chatbot, compromising study reach.

Second, the study relies on self-report for the primary outcome with a 90-day follow-up interval (*Testing*). Patients may not recall test use and maybe less likely to self-report test use after 90 days of requesting a test. However, a 90-day follow-up was chosen to give participants sufficient time to actually use a kit, given that participants could request a test kit regardless of current symptoms and/or exposure, and use the test whenever needed. To maximize response rates, we use two approaches to collect the primary outcome: a quick question via text messaging 90 days after exposure to study interventions and a survey at the end of the study, using multiple contact attempts as well as pre- and post-participation incentives.

Last, the study will be conducted after the peak of the pandemic, when participants may be less motivated to learn about and receive COVID-19 testing. Also, individuals have been overexposed to information about COVID-19 from multiple sources and may have already formed their opinions about COVID-19 and COVID-19 testing. Therefore, it is possible that study findings may not generalize to the context of new onset of a pandemic or outbreak.

Contributorship statement. GDF, BO, TVK, JC, TG, KAK, KK, CYL, CRS, and DWW provided substantial contributions to the conception of the study. All co-authors provided substantial contributions to study design. GDF, BO, TVK, and JC drafted the manuscript. All co-authors reviewed the manuscript critically for important intellectual content. All co-authors provided final approval of the version to be published; and agreed to be accountable for all aspects of the work.

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Competing interests. The authors declare no competing interests.

Data sharing statement. On completion, study data will be made available in compliance with National Institutes of Health data sharing policies. Results will be disseminated through study partners and peer-reviewed publications.

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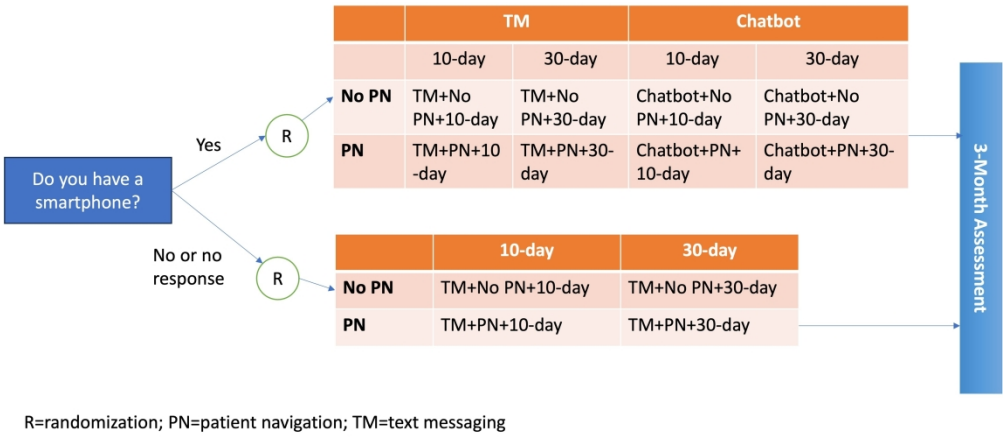

	TM		Chatbot	
	10-day	30-day	10-day	30-day
No PN	TM+No PN+10-day	TM+No PN+30-day	Chatbot+No PN+10-day	Chatbot+No PN+30-day
PN	TM+PN+10-day	TM+PN+30-day	Chatbot+PN+10-day	Chatbot+PN+30-day

	10-day	30-day
No PN	TM+No PN+10-day	TM+No PN+30-day
PN	TM+PN+10-day	TM+PN+30-day

R=randomization; PN=patient navigation; TM=text messaging

Figure 1 – SCALE-UP II Trial Design

327x144mm (300 x 300 DPI)

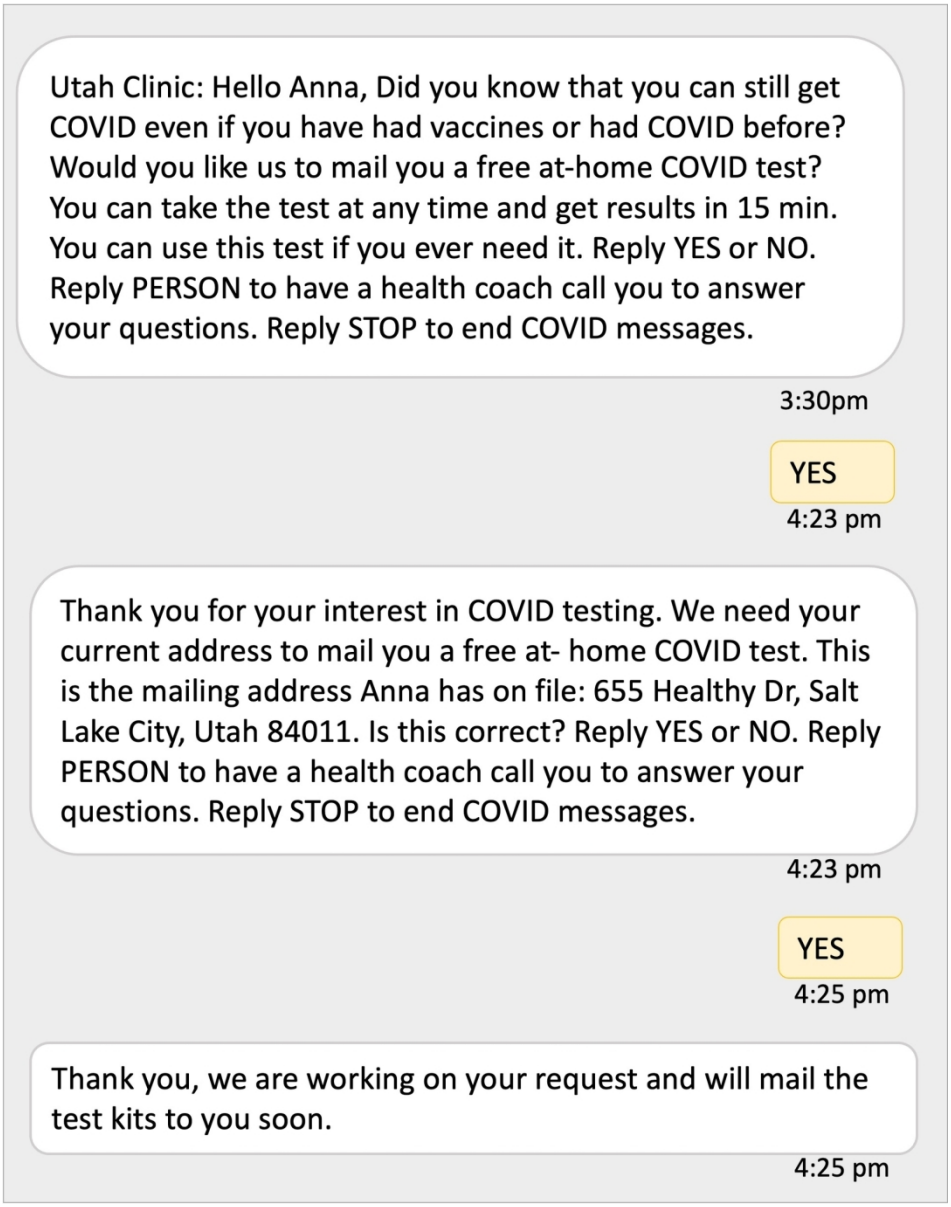

Figure 2 – Sample text message conversation offering COVID-19 at-home testing.

149x188mm (300 x 300 DPI)

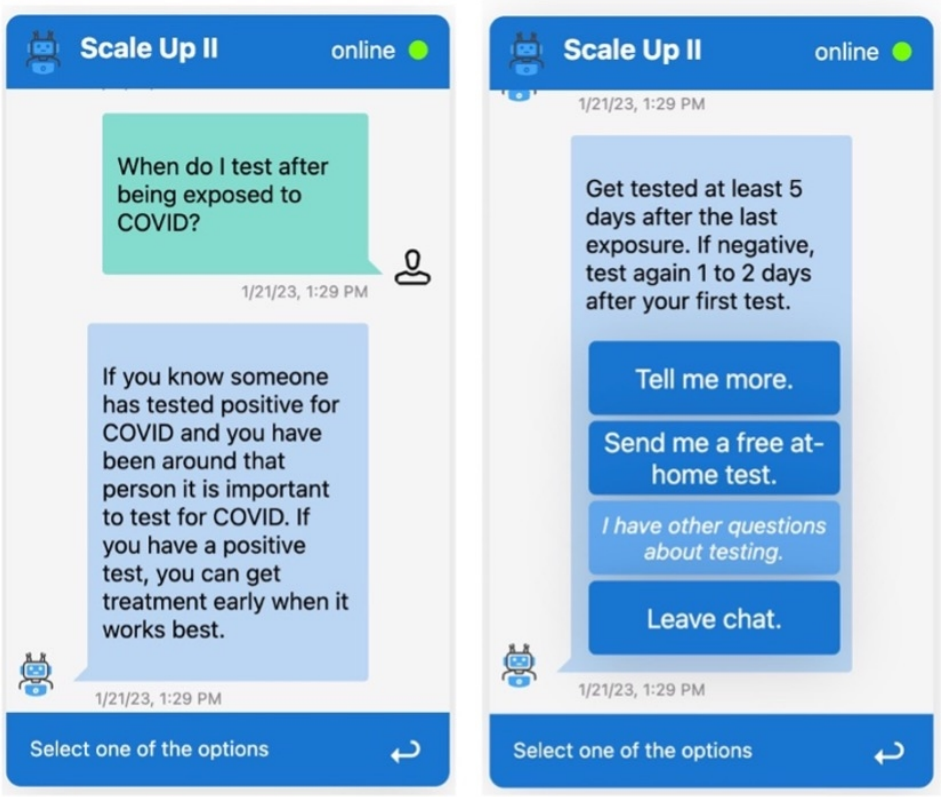

Figure 3 – Sequential screenshot of chatbot intervention showing a question being answered, followed by options to ask further questions, and request a COVID-19 test kit to be mailed to the patient's home.

101x81mm (220 x 220 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	18
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	18
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	5
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4 and 5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	5-7
Objectives	#7	Specific objectives or hypotheses	12
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable,	7

		eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-11
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	NA
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	NA
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-15
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11-12
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who	7-8

		enrol participants or assign interventions	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7-8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7-8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7-8
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-15
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13-15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13-15
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	12-17

Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12-17
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	NA
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	5
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	5
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if	7

		applicable	
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	18
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	2
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	18
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	18
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	supplement
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA