PROJECT TITLE:

COVID-19 Testing in Underserved and Vulnerable Populations Receiving Care in San Diego Community Health Centers

NCT: 05315908

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RESEARCH DESIGN AND METHODS

Community Partner Program and Study Setting

The proposed testing project will leverage existing community health center (CHC)-academic partnerships under the NCI-funded Accelerating Colorectal Cancer Screening and Follow-up through Implementation Science (ACCSIS) Cancer Moonshot grant (UG3CA233314), whose goal is to improve colorectal cancer (CRC) screening among medically underserved populations. This partnership include UCSD and Health Center Partners (HCP) and its subsidiary, Health Quality Partners (HQP). HCP/HQP is a non-profit consortium of 16 CHCs that provide primary care to meet the health needs of communities in Southern California. HCP members collectively operate over 160 clinic sites that include urban, rural, agricultural worker, and US-Mexico border populations, and serve over **858,000 vulnerable patients with 3.6 million patient visits** each year. CHCs have been at the front lines of health care in the nation's poorest neighborhoods for decades. High risk asymptomatic patients served by these centers are not getting proper testing, include essential workers, and could contribute to further spread of the virus. For these reasons, HCP/HQP, our community partner, approached the academic partner with interest in submitting this application.

Participating CHCs. CHC participation involved a process of several presentations that outlined the concept and deliverables and elicited feedback from the medical directors, providers, and staff. Following these, three CHCs indicated interest and capacity to participate: Neighborhood Healthcare (Neighborhood), Vista Community Clinic (Vista), and La Maestra CHC (La Maestra).

Study Methodology

AIM 1*: Compare the effectiveness of automated call vs text messaging for uptake of COVID-19 testing among asymptomatic adult patients with select medical conditions and those 65 years of age and older receiving care at participating CHCs.*

We will include asymptomatic CHC patients with at least one clinic visit in the last year, age 21 years and over, with medical conditions deemed by the Centers for Disease Control and Prevention to increase risk for severe COVID-19 illness[8], including heart failure, coronary artery disease, cancer, chronic kidney diseases, COPD, obesity, sickle cell disease and type 2 diabetes mellitus, and those 65 years of age and older. We estimate that ~40% of CHC patients will have at least one medical condition (~35,000 eligible). We will use our team's extensive experience with existing protocols from our ongoing ACCSIS colorectal screening mailed stool testing intervention as models for the COVID-19 testing project, which have been culturally adapted and tailored for CHC patients.[12,13] CHC staff will mail an introductory letter to eligible individuals describing the importance of COVID-19 testing, inviting them to receive a test, offering opt out instructions, and noting that follow-up contact (phone call, SMS text message) will take place if they do not opt out. Patients who do not opt out, and those whose mail is not returned, will be randomized one week after the introductory letter is mailed.

Randomization. CHC patients will be randomized to one of two arms (see **Figure 2**). Stratification by CHC will not be done due to large sample size.

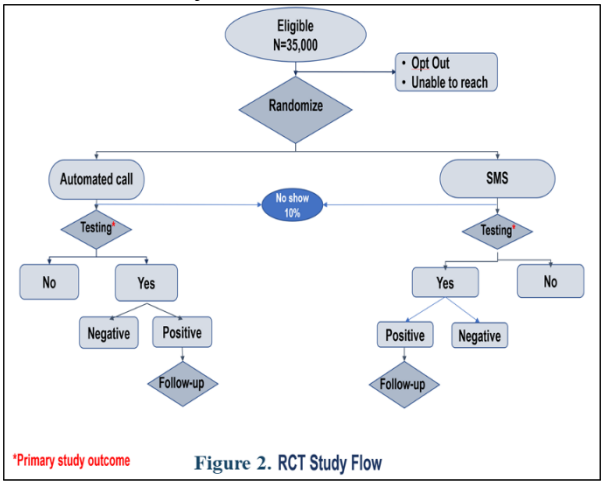

Figure 2. RCT Study Flow

1) Patients in the *Automated call condition* will receive up to two automated phone calls in English or Spanish depending the patients' language indicated in their electronic health record (EHR), between the hours of 10:00am and 9:00pm Monday through Friday.
2) Patients in the *text (SMS) condition* will receive up to two text messages in English or Spanish The automated call and text messaging will instruct patients to call a staff member at the health center's COVID-19 testing center to schedule COVID-19 test.

COVID-19 Testing and Capacity

Randomized patients who are reached will be provided with information on the study and invited to make a clinic appointment for testing. We will use a rapid, high-throughput SARS-CoV-2 qRT-PCR-based diagnostic assay certified for clinical use under FDA Emergency Use Authorization (EUA) that was developed at the UCSD Biochemical Genetics and Metabolomics Laboratory (BCG), a CLIA/CAP certified laboratory. Our process requires 24-48 hours from receipt of samples to reporting of results. Anterior nares swabs will be collected by the patient and placed into automation-ready collection tubes containing PrimeStore Molecular Transport medium, which inactivates pathogens (including the SARS-CoV-2 virus) and stabilizes RNA. We will use Redox middleware to integrate testing laboratory information system (LIS) with the CHC EHR systems. Redox is also set up for required reporting to local, state, and federal agencies through the California Reportable Disease Information Exchange - Electronic Lab Reporting (CalREDIE ELR). Per state guidelines, the testing laboratory is required to report positive and negative test results to the County health department using a standard morbidity report. Positive cases are followed by the County for contact tracing.

Two novel features embedded in this study.

1) In an opportunistic way, we will offer the flu vaccine to patients as part of standard of care at the time of COVID testing. Given recent reports of possible reluctance by individuals to re-engage in health care, including flu vaccination,[14] and with flu season underway, we must prepare for the challenges of its usual dangers combined with novel impacts of COVID-19. This provides an ideal educational opportunity to promote COVID-19 vaccination through positive messaging.
2) We will also assess feasibility and acceptability of COVID-19 testing of study participants' adult household members who are essential workers. When a CHC patient contacts a clinic to make a testing appointment, clinic staff will ask him/her if he/she lives with an essential worker,

as defined by the state of California.[15] If essential workers reside in the home, the participant will be asked if they are willing to refer the household member for COVID-19 testing.

Data Collection, Harmonization and Reporting.

Data collection via EHR and patient surveys will include the PhenX Toolkit core elements including age, sex, race and ethnicity, address, access to health services, income, employment status, education, English proficiency, food insecurity, gender identity, sexual orientation, health insurance, health literacy, and occupation. We will also include household size, foreign-born status, and job type, given that these factors contribute to higher infection rates in Latinx communities,[6] as well as trust in healthcare[16] and discrimination, which are important for our Latinx population. We will work with our advisory board members, community collaborators, stakeholders, the health center leaderships to select additional data elements from the PhenX Specialty collections.

Primary Study Endpoints.

For efficacy assessment, our primary study outcome will be the proportion of patients who undergo testing within one month of initial contact (automated call and text messaging). We will also assess the proportion of patients who undergo testing by the end of the study period (to consider individuals who could not come to the clinic within one month). Secondary endpoints of interest include: number (%) tested (total and by clinic), number (%) infected (total and by clinic). We will also assess the timeliness of testing (from time of contact to testing).

Secondary Study Endpoints.

For flu vaccination, our endpoint will be number vaccinated. For essential worker referral to COVID-19 testing, we will measure *Feasibility* by: a) ascertainment of essential worker status; and b) willingness to offer testing invitation to eligible household member(s). *Acceptability* will be assessed by: a) the proportion of study participants with eligible household members who refer household member(s); and b) the number of household members referred for testing.

Sample Size and Study Power.

Number of study participants was driven by budget, capacity to deliver as many tests as possible, and number of eligible patients at the participating CHCs. Since routine testing of asymptomatic patients is not taking place at the CHCs, we expect that most eligible patients (~35,000) will not be tested. Based on our prior work, we expect ~5% undeliverable calls due to wrong numbers. The exact number of participants randomized in each arm to derive at **9,000 (4,500 per arm)** will be determined by testing uptake rates and an estimated 10% drop off rate due to no shows for testing, with assumption of missing completely at random. To our knowledge, there are no existing data to inform effect size. We thus estimated power for a series of proportion of testing completion between two arms Our study has >80% power with a two-sided alpha=0.05 to detect proportion of testing completion as high as 0.5 in the automated call and 0.7 in the text messaging , and as low as 0.3 and 0.5, respectively, in each corresponding arm.

Statistical Analysis.

Baseline sociodemographic and other clinical characteristics will be assessed for imbalance among the 2 study arms using t-test or chi-square tests for categorical variables. In our primary analysis, we will compare proportion of patients who undergo COVID-10 testing within one month following initiation/randomization between the two study arms using an intention-to-treat approach. For our primary analysis, will use Fisher's exact test for an overall comparison of testing completion between two groups using a $P<.05$ as statistical significant threshold.We will estimate risk ratios and 95% confidence intervals as the measure of association between

intervention groups and testing completion. We will also explore testing rates between groups stratified by social determinants of health factors and other key factors using a likelihood ratio test, recognizing that these analyses will be better suited for the total consortium.

AIM 2: *Gather patient, provider, CHC leadership, and community stakeholder insights to establish best practices for future scale-up of COVID-19 testing sustainability and vaccination.* We will use a mixed-methods approach to evaluate our COVID-19 testing strategies, materials and outcomes (acceptability, feasibility, appropriateness, sustainability). We will gather information on implementation and sustainability facilitators and barriers from individuals receiving/declining testing. Using structured interviews and a coded directed content analysis approach to analyze transcripts, we will collect comparable information for feasibility, acceptability, appropriateness, and sustainability for select providers (1 per clinic), chief medical officers in 3 participating CHCs, and 3 key community stakeholders. Measures include survey items guided by the Practical, Robust Implementation and Sustainability Model (PRISM) and (Reach Effectiveness, Adoption, Implementation and Maintenance) RE-AIM framework, and include the Feasibility of Intervention Measure (FIM), Acceptability of Intervention Measure (AIM), and Intervention Appropriateness Measure (IAM).