Use of Behavioral Economics in Repeat SARS-CoV-2 Antibody Testing in Disadvantaged Communities

Protocol Number: 3R33AG057395-04S1

Principal Investigator:

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Sponsor:

The National Institute of Aging

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CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH terms of award.

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STATEMENT OF COMPLIANCE

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

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

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

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

INVESTIGATOR'S SIGNATURE

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

Principal Investigator or Clinical Site Investigator:

Signed: Jason Doctor Date: 11/13/2020

Name*: Jason Doctor, PhD

Title*: Professor

Investigator Contact Information

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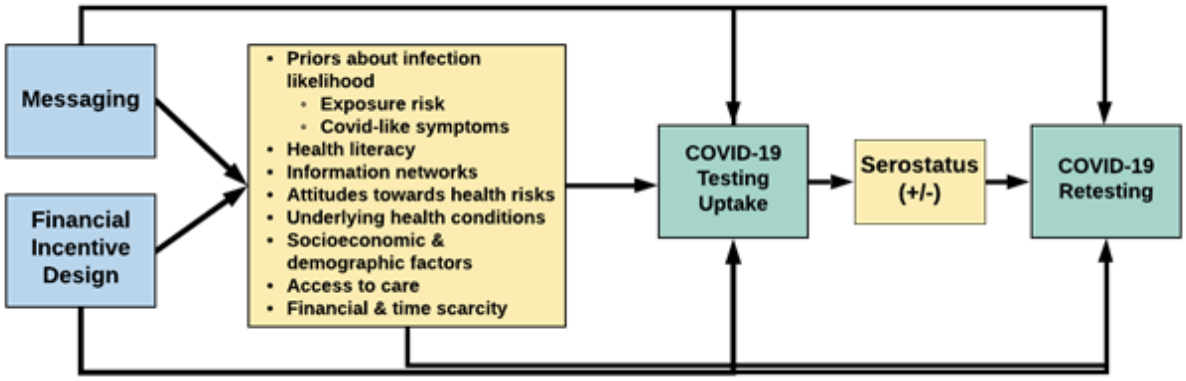
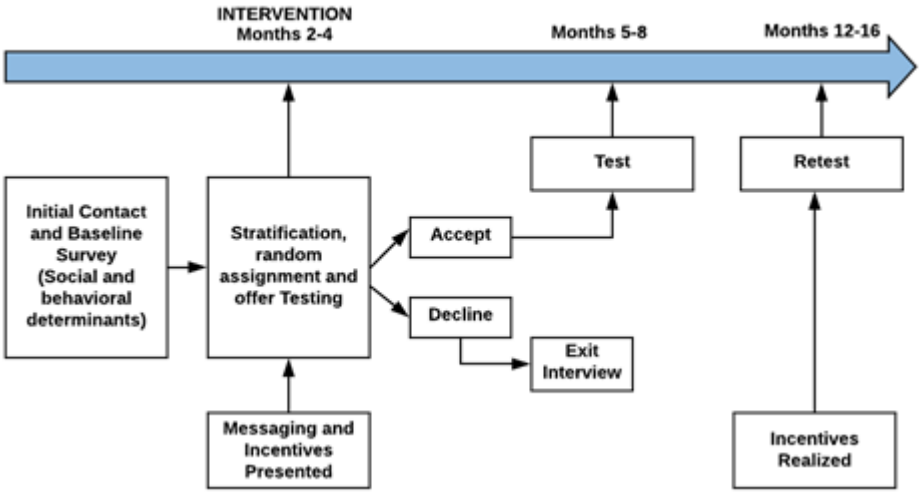
1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Use of Behavioral Economics in Repeat SARS-CoV-2 Antibody Testing in Disadvantaged Communities
Grant Number:	3R33AG057395-04S1
Study Description:	Uptake of SARS-CoV-2 testing in underserved populations is subject to barriers related to resources and behaviors that may differ within communities and even households. Testing for SARS-CoV-2 antibodies in underserved populations can play an important strategic role. It is important to understand barriers and actionable facilitators of testing in underserved populations to address those most in need.
Objectives*:	Primary Objective: This project aims to evaluate the effectiveness of risk-based messaging and incentives that promote repeated testing for SARS-CoV-2 antibodies. Secondary Objectives: To understand social and behavioral determinants of COVID-19 testing and variations within sub-groups of this population.
Endpoints*:	Primary Endpoint: Characterize barriers to access, bias, risk attitude and incentive preferences through outreach and survey responses. Secondary Endpoints: Identify groups that may partition facilitators to testing into minimal and maximal effectiveness. Evaluate interventions and their heterogeneous treatment effects on social determinants and address barriers to test participation in a randomized trial.
Study Population:	2,160 individuals (540 families) from the largest Federally Qualified Health Center (AltaMed Health) in Los Angeles, California.
Phase* or Stage:	Stage III clinical trial
Description of Sites/Facilities Enrolling Participants:	AltaMed Health Services is one of the largest qualified health centers in the United States. The Commerce clinic site will be a participating site enrolling participants. The study does not intend to include sites outside of the United States.
Description of Study Intervention/Experimental Manipulation:	Using a random sample of households, we will recruit participants to conduct a randomized 2 x 2 (Messaging x Incentive) factorial experiment, in which participants complete a comprehensive set of social and behavioral surveys to identify determinants of commitment to testing.
Study Duration*:	24 months
Participant Duration:	12 months

1.2 SCHEMA





1.3 SCHEDULE OF ACTIVITIES

Assessment	Screening: Baseline	Baseline, Enrollment,	Intervention start:	Intervention end:	Follow-up period:
	(Month -3 to Month 0)	Randomization: (Day 1)	(Month 1)	(Month 6)	(Month 7 to Month 12)
Patient-level Assessments					
Informed Consent Form		X			
Demographics			X		
Inclusion/Exclusion Criteria	X	X			
Social Determinants of Health Survey		X		X	
Visit-level assessments					
Antibody Testing			X	X	

Adverse Events			X	X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

SARS-CoV-2 virus has created one of the most challenging public health emergencies in modern history and antibody testing could be an important tool for responding to this pandemic. Uptake of SARS-CoV-2 testing in underserved populations is subject to barriers related to resources and behaviors that may differ within communities and even households. Testing for SARS-CoV-2 antibodies in underserved populations can play an important strategic role for several reasons. First, antibody testing is critical for public health surveillance and planning as it can identify both active and recovered infections. This helps us identify the extent of exposure in the community and learn more about illness severity and the mortality rate. This is crucial information for policy makers as they plan pandemic response to reduce disease burden and disparities. Second, antibody testing is also an important clinical tool and providers can choose from several FDA approved antibody tests with high specificity and sensitivity.[1] Finally, although the science is still uncertain, antibody testing might be used as a tool for identifying populations that can safely return to work or for prioritizing scarce PPE resources. However, antibody testing to date in the US has been limited. It is important to understand barriers and actionable facilitators of testing in underserved populations to address those most in need. We need to understand how to increase uptake of testing among vulnerable populations and how to encourage testing and retesting in general. Messaging, financial incentives, social and personal factors as well as the effect of learning of your first test results have implications for controlling the spread of the virus. A negative test result might promote prevention behaviors for people who thought they were previously infected.[2]

Our study, which will enroll and track a representative cohort of 2,160 persons (540 family clusters) for SARS-CoV-2 antibodies and repeatedly test them for antibodies, is significant for several reasons. First, it will allow us to track the evolution of the pandemic in the largest federally qualified health center (FQHC) in the United States. Second, we will be able to observe how the risk of infection is evolving differently in low-income underserved populations as compared to the general population. Third, repeat antibody testing of those who were seropositive in the first wave of testing will allow us to test how well antibodies maintain their presence at a second test 6-months later. There is preliminary evidence that antibodies wane over time, however current evidence is limited to few studies and small sample sizes.[3] Fourth, and most importantly for scalable, generalizable, findings, we will find actionable ways to motivate repeat testing and we will be able to tailor those ways to the social and behavioral characteristics of the persons being tested.

2.2 BACKGROUND

In a prior study,[2] we asked people on a 10-point scale how likely they were to have had COVID-19. About 20% of the sample reported 7 or higher on this 10-point scale, however only 4% of the sample tested positive. This suggests antibody testing has a large potential to correct beliefs about past infection and promote retesting for those who are antibody negative. However, a positive test could potentially reduce willingness to participate in repeat testing. Among those who tested positive, about 23% of the sample reported a 1 or 2 on a 10-point scale on how likely they were to have had COVID-19. These people may be less likely to retest for studies trying to depict the immune response over time. Underserved populations face different barriers to testing and these may vary within different communities and households. The diversity in Los Angeles allows us to assess how barriers to antibody testing differ for vulnerable groups. Data from our prior study show that Blacks and Latinos were 27 percentage points and 14 percentage points less likely to participate in testing compared to their white counterparts.[2] We also find that those with household income less than $50,000 were 17 percentage points less likely to take-up antibody testing compared to those with household income greater than $100,000. It is important to understand why these disparities exist. The proposed research will shed light on this issue by evaluating barriers/facilitators of testing including

beliefs about COVID-19, mistrust of healthcare, insurance, and cultural factors. More importantly, we will study the behavioral, social and cultural factors that make actionable facilitators minimally and maximally effective. Many individuals may react differently to antibody test results. Our preliminary analysis suggests that the reactions to test results vary across subgroups. For example, lower income families and minorities are more likely to test positive, but less likely to think they have already had COVID-19. This mismatch between beliefs and serostatus might imply lower motivation to receive testing. Similarly, a larger portion of Blacks and Latinos are low-income, and many cannot work from home. A positive antibody test could have a larger increase in economic activity for this population if their perceived risk of leaving the house for work is reduced. This study will allow for improved understanding of the factors contributing to uptake of COVID-19 testing in underserved populations, and enhance our understanding of public health and health behaviors.[2]

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

The potential risks associated with participation in this study include 1) disclosure of survey responses, 2) disclosure of test results and 3) small levels of discomfort from a needless blood draw. It is also possible that participants do not know how to interpret their results, which could cause anxiety or undue reductions in prevention behavior. The antibody test involves a skin prick on rare occasion lead to prolonged bleeding. People who take medicines called blood thinners may have some bleeding from the site for a short time after the test is over.

2.3.2 KNOWN POTENTIAL BENEFITS

All participants will receive free serology testing. Demand for testing is very high and tests are relatively expensive. In addition, accurate knowledge of serostatus is a benefit for participants. If participants increase preventative behavior in response to antibody testing then the research will also benefit others in society by reducing the spread of COVID-19.

Answering the research questions for this study is critical for designing effective and equitable COVID-19 testing programs. This study will help understand the barriers to serology testing, which will be important as serology increasingly used to inform policy. It will also help the world understand how people respond to learning their serology test results, which will help us better understand how best to use testing as a policy tool. Finally, it will provide important evidence on how antibodies wane after acute exposure, how long they remain in the system, and whether people can be re-infected. In sum, the risks of this study are small relative to the potential benefits in identifying active and recovered COVID-19 infections for public health planning.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

We will take great measures to protect against the risks highlighted above.

1. Protections against disclosure risks: Disclosure of survey responses or test results is highly unlikely. The CLIA lab will only have participant study ID and specimen barcode; they will not have any patient identifying information. Data will be recorded with SSL protected web sites to a data warehouse, and transferred over secure network protocol. Data will be kept in a HIPAA compliant version of REDCap and in encrypted files on a secure research computing cloud at USC Schaeffer Center facilities.
2. Protections against risks associated with learning results: All participants will receive a debrief after each serology test to inform them of what their test results mean for them. Communication of test results will align with the Abbott assay Fact Sheet provided by the FDA. The results communication will also follow CDC guidelines which suggest that individuals should continue preventive behaviors irrespective of test results and those who are symptomatic should obtain PCR test to check for active infection. We will also

have a hot-line that participants can call if they have any questions about their results and what they mean.

Answering the research questions for this study is critical for designing effective and equitable COVID-19 testing programs. This study will help understand the barriers to serology testing, which will be important as serology increasingly used to inform policy. It will also help the world understand how people respond to learning their serology test results, which will help us better understand how best to use testing as a policy tool. Finally, it will provide important evidence on how antibodies wane after acute exposure, how long they remain in the system, and whether people can be re-infected. In sum, the risks of this study are small relative to the potential benefits in identifying active and recovered COVID-19 infections for public health planning.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
To evaluate the effectiveness of risk-based messaging and incentives that promote repeated testing for SARS-CoV-2 antibodies	Main effect of incentives, the main effect of messaging strategy, and the interactions between incentives and messaging and covariates; seropositive status	We have found that providing at-risk incentives that can be insured with repeat health behavior outperforms direct cash payments of the same expected value.
Secondary		
To understand social and behavioral determinants of COVID-19 testing and variations within sub-groups of this population.	Characterize barriers to access, bias, risk attitude and incentive preferences through outreach and survey responses. Identify groups that may partition facilitators to testing into minimal and maximal effectiveness.	covariates

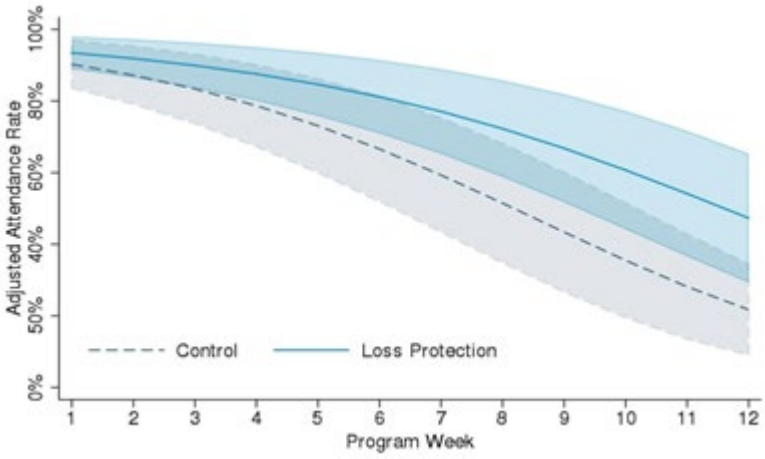
4 STUDY DESIGN

4.1 OVERALL DESIGN

Social determinants need to be understood in the context of actionable facilitators (things COVID-19 policymakers can do) to encourage repeat testing. We will study two types of facilitators (messaging and financial incentives) and evaluate the heterogeneity of treatment response based on the characteristics of those tested. We will conduct a 2 x 2 (messaging x financial incentive) factorial design (Aim 3) that stratifies on social and behavioral determinants (Aim 2) collected as part of an initial survey (Aim 1). We have been studying ways to identify powerful incentives for repeated health behaviors. We have found that providing at-risk incentives that can be insured with repeat health behavior outperforms direct cash payments of the same expected value. Individuals were 70% more likely to return to a health screening when insuring against losing a baseline incentive than they were when paid cash ($p < 0.01$). [4] In addition, in a recent study we showed that disadvantaged patients at a federally-qualified health center were more likely to repeat a health behavior twice each week over 12 weeks when repetition

was insuring against losing a weekly incentive than if they were paid equivalently in cash (see Figure 1; $p < 0.05$). [5]

Figure 1. Insurance (loss protection) vs. cash (control) incentive for repeat health behavior among disadvantaged persons (N = 151)



2 x 2 Stratified Randomization

Messaging (Factor 1): We will develop simple messaging that frames the decision to test in terms of either: (i)family risk, or, (ii) personal risk. These methods will be piloted, but will be of the form "Antibody testing will help you understand your family's risk of getting COVID-19"; and, "Antibody testing will help you understand your risk of getting COVID-19". Family risk framing may engender concern for loved ones. It may also make it easier to mentally simulate family burdens with COVID-19 such as knowing how several people in the family becoming sick could adversely affect the lives of everyone in the family. We hypothesize that the family framing will result in greater uptake of testing and greater repeat testing.

Incentives (Factor 2): We have been studying incentives for repeat testing since 2015. [4] We have found that low-income persons respond better to insuring at-risk rewards with repeat behavior than they do to cash payment. [5] For example, suppose for your first test you are given as an incentive that offers an 80% chance of winning $52. You then are told you can guarantee winning this lottery by having a second COVID-19 test in 8-months. This is preferable to a $10 cash payment (i.e., the cost of the insurance against losing an 80:20 bet on $52) in 8-months. To low-income persons, delivering an attractive lottery incentive for baseline testing and then letting persons insure this lottery with repeat testing may better encourage retesting by giving peace-of-mind and relieving them of worrisome distractions about money that they may already face. We will construct two incentives for this factor: (i) a baseline incentive offering a 90% chance of $60; (ii) a repeat financial incentive. For (ii) Group 1 receives insurance on winning the baseline incentive; Group 2 receives a lottery incentive offering a 1 in 25 chance of winning $150. The expected reward for both Group 1 and 2 for having completed both baseline and retest is $60 (i.e., program costs are the same). In prior work, we've shown that insuring against losing a lottery was more effective than cash payments in the cost of insurance. Here we explore if this also holds true against low-probability and high-reward lotteries for which people may be optimistic about winning.

Messaging and incentives may interact. For example, thinking about the safety of your family after a family-framed message may make insuring against losing a lottery more attractive than another risky lottery.

Testing in a Diverse Population: Sampling low-income populations is important for research on disparities, however, recruiting this population is challenging because they often lack consistent contact information, do not have internet access, and mistrust research. We will use a novel way of recruiting this population by partnering

with AltaMed Health Services, the largest FQHC in the United States that serves overwhelmingly a low-income and minority population. Partnering with an FQHC will build trust and also provide us access to reliable contact information. In a pilot study, we were able to recruit over 50 families for antibody testing within just 2 days at a local FQHC. AltaMed Health Services is our partner on our parent grant R33 AG057395; we have worked with them for over 10 years. We will work with the AltaMed Patient Centered Research Advisory Committee (PC-RAC) which is committed to ensuring that all research conducted within or in collaboration with AltaMed addresses patient and community needs. This committee aims to create a research program that is responsive to patient priorities and concerns, emphasizes community-based participatory research principles, and assures research findings improve patient health through strategic program and policy recommendations to promote economic, social, and racial justice. The PC-RAC is administered through AltaMed's Health Equity and Access for Latinos (HEAL) project whose mission is to develop a patient/community engaged research process. We will recruit two patients who have tested positive for COVID-19 to supplement this existing group. The Community Advisory Board will meet quarterly for this project to inform the development of study materials and review findings.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

Repeat testing for SARS-CoV-2 antibodies in disadvantaged communities will help identify active and recovered infections over time, and, as we learn about antibody protection, it may help identify persons who have immunity. Many questions about social barriers and behavioral facilitators remain unanswered.

4.3 JUSTIFICATION FOR INTERVENTION

Social determinants need to be understood in the context of actionable facilitators (things COVID-19 policymakers can do) to encourage repeat testing. We will study two types of facilitators (messaging and financial incentives) and evaluate the heterogeneity of treatment response based on the characteristics of those tested. We will conduct a 2 x 2 (messaging x financial incentive) factorial design (Aim 3) that stratifies on social and behavioral determinants (Aim 2) collected as part of an initial survey (Aim 1). We have been studying ways to identify powerful incentives for repeated health behaviors. We have found that providing at-risk incentives that can be insured with repeat health behavior outperforms direct cash payments of the same expected value. Individuals were 70% more likely to return to a health screening when insuring against losing a baseline incentive than they were when paid cash ($p < 0.01$).[4] In addition, in a recent study we showed that disadvantaged patients at a federally-qualified health center were more likely to repeat a health behavior twice each week over 12 weeks when repetition was insuring against losing a weekly incentive than if they were paid equivalently in cash (see Figure 1; $p < 0.05$).[5]

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed the baseline assessment, participated in antibody testing and the 6-month follow-up assessment. Participants will be debriefed at the end of the study.

The end of the study is defined as completion of the 6-month follow-up assessment shown in the Schedule of Activities [(SoA), **Section 1.3**].

5 STUDY POPULATION

Our study population will consist of patients on the registries of AltaMed's 12 Los Angeles County primary care clinics, and we will draw a simple random sample of 1000 patient households without replacement. Patients will be randomly selected by address and confirmed to be patients by medical identification number. All members of

the household, both adults and children over the age of 5, are invited to participate in testing, but at least one parent and one child must participate in order for the household to qualify. Partnering with FQHCs will build trust and also provide us access to reliable contact information. In a pilot study at a FQHC, we were able to recruit over 50 families for antibody testing within just 2 days.

5.1 INCLUSION CRITERIA

We will use simple random sampling within the AltaMed patient registry to identify AltaMed patients (and family members) for study recruitment. Adults and children 5 years of age and older will be invited to participate.

5.2 EXCLUSION CRITERIA

Children under 5 years of age will be excluded from the study.

5.3 LIFESTYLE CONSIDERATIONS

Not applicable

5.4 SCREEN FAILURES

Not applicable

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Our study population will consist of patients on the registries of AltaMed's 12 Los Angeles County primary care clinics, and we will draw a simple random sample of 1000 patient households without replacement. Patients will be randomly selected by address and confirmed to be patients by medical identification number. All members of the household, both adults and children over the age of 5, are invited to participate in testing, but at least one parent and one child must participate in order for the household to qualify.

Potential study participants must meet the inclusion criteria prior to enrollment. We will use stratified random sampling within the AltaMed patient registry to identify AltaMed patients (and their family members) for study recruitment. Stratification will be by distance to the testing site: using zipcodes, we identified the median distance of patients empanelled in any Los Angeles County AltaMed clinic to the testing site, and we then identified roughly equal random samples of those living less than this median distance (n=3148) and those living more than this median distance (n=3074). In contacting individuals in this sample, all adults and children 5 years of age and older will be invited to participate in testing; at least one adult and one child from a household must be willing to participate in order to be eligible for testing.

Only one adult member (head of household) will be completing the survey. Minors will not be completing survey questions. Children under 5 years of age will be excluded from the study as Tasso SST devices are not recommended for children under 5.

Study participants will be recruited via phone by a culturally competent, bilingual research coordinator from The Henne Group. Consent for participating in the study will be a two-part process. As part of the initial recruitment call, The Henne Group callers will describe the study and ask adult (head of household) if they would like to participate in a survey about COVID-19 and social determinants of health. Consent to participate

in the survey will be verbal during the phone call. Participants will be informed of the survey data sharing with Duke Clinical Research Institute, and that signed consenting for DCRI data sharing and antibody testing will occur at the time of the in person appointment. They will be informed that if they do not make it to their appointment for some reason, their survey responses will be not shared with DCRI but the study team at USC will use the deidentified survey information to better understand how behaviors and beliefs may impact testing decisions. Participants who decline participation will be asked for reasons why they declined.

Adult participants who provide verbal consent for the survey will complete the baseline survey, a one time survey which takes approximately 20-30 minutes to complete. Survey responses will be documented in the participant's REDCap record. After the baseline survey is completed, participants and their family members will be scheduled for antibody testing at a time convenient for them. After the baseline survey is completed we will ask if the participant is interested in participating in testing. If yes, the coordinator will explain the risk and benefits of testing. S/he will also inform participants that if they accept testing they will receive a lottery ticket that carries a 90% chance of winning $60 provided they complete their first test; and that for retesting they will receive either insurance on their initial lottery ticket or will be given an addition lottery ticket with a 4% (1 in 25) chance of winning $150. Each participant who consents to participate in the baseline survey will receive an incentive payment of $10 and each participant who completes at least one test will have their lotteries played. Participants who consent for baseline survey but decline testing will be asked for reasons why they declined.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

We will study two types of facilitators (messaging and financial incentives) and evaluate the heterogeneity of treatment response based on the characteristics of those tested. We will conduct a 2 x 2 (messaging x financial incentive) factorial design that stratifies on social and behavioral determinants collected as part of an initial survey. We have been studying ways to identify powerful incentives for repeated health behaviors. We have found that providing at-risk incentives that can be insured with *repeat* health behavior outperforms direct cash payments of the same expected value. Individuals were 70% more likely to return to a health screening when insuring against losing a baseline incentive than they were when paid cash ($p < 0.01$).[4] In addition, in a recent study we showed that disadvantaged patients at a federally-qualified health center were more likely to repeat a health behavior twice each week over 12 weeks when repetition was insuring against losing a weekly incentive than if they were paid equivalently in cash.

Messaging (Factor 1): We will develop simple messaging that frames the decision to test in terms of either: (i) *family risk,* or, (ii) *personal risk*. These methods will be piloted, but will be of the form "Antibody testing will help you understand your family's risk of getting COVID-19"; and, "Antibody testing will help you understand your risk of getting COVID-19". Family risk framing may engender concern for loved ones. It may also make it easier to mentally simulate family burdens with COVID-19 such as knowing how several people in the family becoming sick could adversely affect the lives of everyone in the family. We hypothesize that the family framing will result in greater uptake of testing and greater repeat testing.

Incentives (Factor 2): We have been studying incentives for repeat testing since 2015.[4] We have found that low-income persons respond better to insuring at-risk rewards with repeat behavior than they do to cash payment.[5] For example, suppose for your first test you are given as an incentive that offers an 80% chance of winning $52. You then are told you can guarantee winning this lottery by having a second COVID-19 test in 8-months. This is preferable to a $10 cash payment (i.e., the cost of the insurance against losing an 80:20 bet on $52) in 8-months. To low-income persons, delivering an attractive lottery incentive for baseline testing and then letting persons insure this lottery with repeat testing may better encourage retesting by giving peace-of-mind and relieving them

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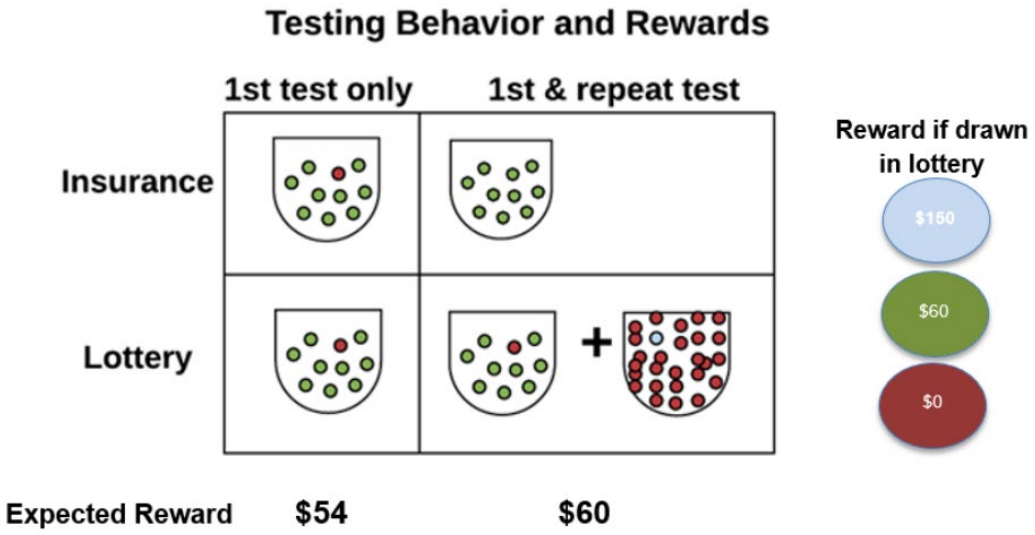


6.1.2 ADMINISTRATION AND/OR DOSING

Clinical research coordinators will be blinded to the participant's condition. Participants will receive information on the intervention arm as part of the initial recruitment phone call and will also receive a reminder at the time of initial test visit. This will be provided as either a sealed envelope or email/text (based on participant preference) with test return instructions and information on the incentive they will be receiving. Lotteries will be played and incentives paid at the time of Wave 2 retesting.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

All recruitment callers will be trained on the randomization process and the relevant scripts household members should receive depending on intervention arm assignment. CRCs are blinded to intervention assignment; site monitors will cross check intervention assignment and ensure participants are getting correct reminder instructions.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Randomization will occur at the beginning of the study using the following steps:

- We will receive a list of 6,222 names from AltaMed Health Services (3074 in the "far" group and 3148 in the "near" group; "far"/"near" based on further/nearer than the median distance of LA AltaMed patient zip codes from the testing site's zip code).
- Using this list, The Henne Group will reach out to these participants asking if they would like to participate in the study and have a child in the household.
- Each household will be assigned a study ID; each participant will have a Study ID number as well as a medical record number (for patients only) from AltaMed to incorporate into the EHR.
- A list of eligible participants will be available in our HIPAA compliant version of REDCap with their name, research ID and script option (4 options- 2 for messaging/ 2 for financial incentives)
- Using the randomization feature in REDCap, we will be able to randomize the scripts that each participant will receive.

- Onsite Clinical research coordinators will be blinded to the participant's condition.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Participants adherence to Wave 2 retesting will be tracked via REDcap.

6.5 CONCOMITANT THERAPY

Not applicable

6.5.1 RESCUE THERAPY

N/A.

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Participants who decline testing initially will be offered an exit survey which will ask them for reasons for declining. We will longitudinally follow the initial cohort that completed baseline survey (including people who declined testing in wave 1) and offer an additional wave of testing 6 months after the first wave.

Participants can choose to withdraw from the study at any time, and this will be documented in their REDCap record. When a subject discontinues Wave 2 retesting but not from the study, remaining study procedures (data analysis) will be completed as indicated by the study protocol.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request. The reason for participant discontinuation or withdrawal from the study will be recorded in REDCap. Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced.

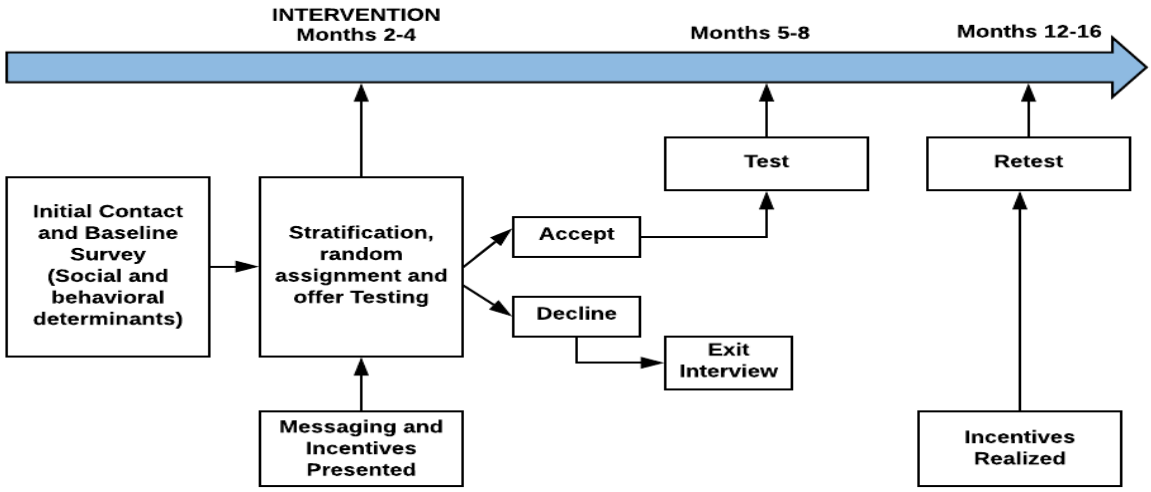
7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to respond to request for Wave 2 retesting after at least 3 attempts. Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Households who are interested in participating will be assigned a household ID, and one adult from each household will complete the study survey questions. Household members interested in testing will then be assigned a unique Study ID and be scheduled for a testing appointment at a date and time convenient for them. Participants will be called with antibody test results within 5-7 days of initial test. Six months following initial test, participants will be asked to come in for Wave 2 retesting, where lotteries will be played and incentives realized. Participants will be called with antibody test results within 5-7 days of second test All decisions related to participation and the scheduled appointment times will be documented within REDCap.



8.2 SAFETY ASSESSMENTS

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any adverse events for participants. Unanticipated Problems that are unexpected, related or possibly related to this research (including anywhere there is a reasonable possibility that the incident or outcome may have been caused or associated with the study) and that suggests that the research places patients at greater risk of harm than was previously known or recognized will be thoroughly and promptly investigated.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any serious adverse events for participants and therefore SAE reporting is not applicable.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any serious adverse events for participants and therefore SAE reporting is not applicable.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any serious adverse events for participants and therefore SAE reporting is not applicable.

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Not applicable

8.3.3.3 EXPECTEDNESS

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any adverse events for participants.

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

Not applicable

8.3.5 ADVERSE EVENT REPORTING

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any adverse events for participants.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

Because this study involves COVID-19 serology testing involving only a skin prick (FDA approved Tasso device) to collect the sample, we do not anticipate any serious adverse events for participants.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

Not applicable

8.3.8 EVENTS OF SPECIAL INTEREST

Not applicable

8.3.9 REPORTING OF PREGNANCY

Not applicable

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

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

8.4.2 UNANTICIPATED PROBLEMS REPORTING

Unanticipated Problems that are unexpected, related or possibly related to this research (including anywhere there is a reasonable possibility that the incident or outcome may have been caused or associated with the study) and that suggests that the research places clinicians or patients at greater risk of harm than was previously known or recognized will be thoroughly and promptly investigated. The Unanticipated Problem will be investigated, formally written down with a corrective plan and measures to prevent reoccurrence. This report will be shared with the NIA Program Officer within 48 hours of study's knowledge of the problem.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Not applicable

9 STATISTICAL CONSIDERATIONS

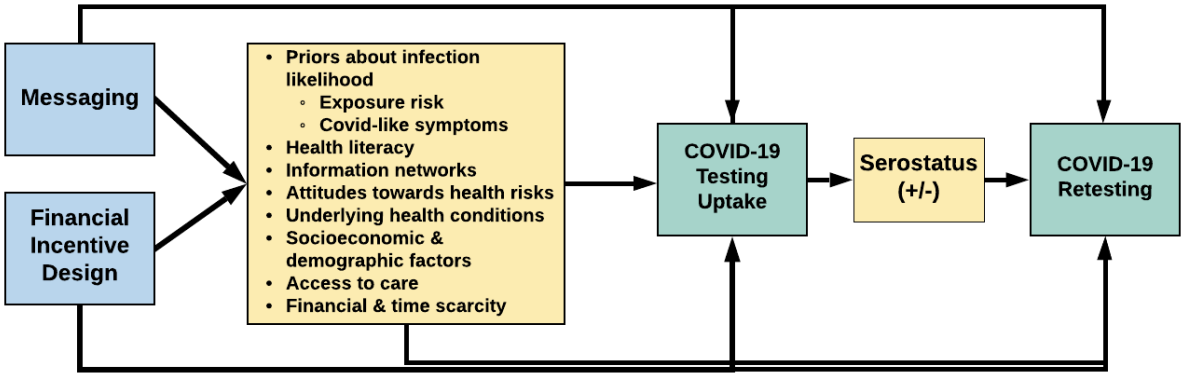
9.1 STATISTICAL HYPOTHESES

The figure below provides a conceptual diagram for thinking about what factors may influence testing take-up and retesting. Testing take-up would depend on several factors, including prior beliefs about infection, health literacy, information networks, health conditions, demographics and socio-economics. We have the following hypothesis based on analysis of literature on testing for HIV and Hepatitis as well as preliminary analysis of data from our prior study:

Hypothesis 1: Those who believe that they have been infected in the past would be more likely agree to testing to confirm that they have antibodies and potential immunity**; Hypothesis 2:** People with poor health literacy will be less likely to agree to testing as they might find it daunting to understand what the test does and how to interpret results**; Hypothesis 3:** Those who are risk averse would be more likely to agree to testing as it reduces uncertainty about serostatus; **Hypothesis 4:** Those with preexisting health conditions would be more likely to agree to testing as they face higher risks from COVID-19 and thus have more to gain from learning serostatus; **Hypothesis 5**: Minorities and those in lower socio-

economic strata would be less likely to agree to testing due to fear of discrimination, lack of trust in health care/research, poor past experience, and perception of being at low risk of infection. We also generate hypotheses for facilitators to retesting (r) relative to those who take a first test **Hypothesis 1r:** Persons who practice low COVID-19 mitigation, exhibit risk-seeking and have high exposure risk may respond to a lottery retest incentive. **Hypothesis 2r:** Those persons with low income, unemployed, or have high stress or anxiety may respond most to insurance of incentives. **Hypothesis 3r**: Persons who are sero+ at baseline will be less likely to return for a retest. **Hypothesis 4r:** Lottery insurance and family messaging will induce higher retesting rates. Hypotheses 1-5 are covariates that may affect agreeing to the test. Hypotheses 1r and 2r refer to heterogeneity of treatment effects for retesting, while 3r and 4r are main effects on retesting.

Conceptual diagram



9.2 SAMPLE SIZE DETERMINATION

We will recruit a cohort of 2,160 people (540 families), and stratify into 3 subgroups based on predictors of commitment to participation in testing programs. Randomization will be clustered by family. Sub-group membership will be based on the mean household survey response to the survey component. For the purposes of power analyses, we assume high Intra Cluster Correlation within family on uptake of repeat testing (>0.90).

Stratified Allocation Plan and Power Analysis (540 households, 2160 individuals)		
	Control	Intervention
Stratification	**# households**	**# households**
HTE Subgroup 1	60	60
HTE Subgroup 2	60	60

HTE Subgroup 3	60	60
% Seropositive in Baseline Test	**10%**	**10%**
Total Households Per Arm	**180**	**180**
Projected Average Treatment Effect Size	Reference Group	Reference+10%
Minimum Detectable Effect Size Compared to Controls (H4r)	±3%	
Detectable 3-subgroup HTE and Seropositivity (H1r, H2r, H3r)	±7%	

Assuming a similar effect size to prior studies in similar populations, we expect a 10 percentage point difference in repeat testing adherence between intervention and control groups. With 540 households, we are powered to detect as little as 3 percentage point difference between interventions and controls in the 540 households we will enroll. To assess heterogeneity of treatment effects (THE), there is more than 80% power to detect a between-subgroup difference of 7 percentage points, assuming 180 households in each sub-group.

9.3 POPULATIONS FOR ANALYSES

Sampling low-income populations is important for research on disparities, however, recruiting this population is challenging because they often lack consistent contact information, do not have internet access, and mistrust research. We will use a novel way of recruiting this population by partnering with AltaMed Health Services, the largest FQHC in the United States that serves overwhelmingly a low-income and minority population Partnering with an FQHC will build trust and also provide us access to reliable contact information.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Aim 1 (Hypotheses 1-5): Data from the baseline survey combined with data on which heads of households attended Time 1 testing will be used to address Aim 1. In particular, we will estimate logistic regressions where the dependent variable will be the binary indicator whether the head of household attended Time 1 testing (yes vs. no). The key independent variables will include:1) prior COVID-19 testing, 2) which SARS-CoV-2 information sources are most trusted, 3) risk aversion, 4) heads of households or family member diagnosis of a health condition (e.g., diabetes, hypertension) and, 5) race/ethnicity, income, discriminatory incidences, household receipt of Supplemental Nutrition Assistance Program (SNAP) or Supplemental Security Income (SSI) benefits, and citing money as the biggest vaccine barrier.

$$\pi = \beta_0 + \beta_1 x_i + \varepsilon_i \quad [1]$$

$\pi = ln\left(\frac{p}{1-p_{ji}}\right)$; p_i, is the probability of attending Time 1 testing, by head of household *i,* and β_1 is each head of household reported social determinant of health. This will allow us to identify significant social and behavioral determinants for heterogeneity of effects (currently hypothesized in Hypotheses 1-5 above).

Aim 2 (Hypotheses 1r-4r): Aim 2 will involve regressing Time 2 retesting (yes vs. no) on the following items for Hypotheses 1r-4r: 1r) risk aversion, essential worker status, access to personal protective equipment, and risky forms of transportation (e.g., personal vehicle, carpool, bus), 2r) income, discriminatory incidences, employment status, whether heads of households personally, or other family members suffer from depression and/or mental health issues, and household receipt of Supplemental Nutrition Assistance Program (SNAP) or Supplemental Security Income (SSI) benefits, 3r) Time 1 seropositivity status and, 4r) the Financial Incentive and Messaging study arms.

$$\pi = \beta_0 + \beta_1 x_i + \beta_2 x_i + \beta_3 x_i + \varepsilon_i \quad [2]$$

For Hypotheses 1r-2r, $\pi = ln\left(\frac{p}{1-p_{ji}}\right)$, is the probability of Time 2 attendance by head of household *i* given they attended Time 1 testing; β_1 is the main effect of the head of household reported characteristic, β_2 is the main effect of the Financial Incentive, where the lottery condition is the reference, and β_3 is the interaction between the head of household reported social determinant of health and Financial Incentive.

$$\pi = \beta_0 + \beta_1 x_{ij} + \eta_j + \varepsilon_i \quad [3]$$

For Hypothesis 3r, we will use a simple mixed-effects logistic model, where $\pi = ln\left(\frac{p}{1-p_{ji}}\right)$, is the probability of Time 2 attendance by individual *i* in household *j* given they attended Time 1 testing; $\beta_1$is seropositivity status at Time 1 (yes vs. no); and η_j is the random intercept for each household capturing household-level effects.

We will use two separate models for Hypothesis 4r.

$$\pi = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij} + \beta_3 x_{ij} + \beta_4 x_{ij} + \beta_5 x_{ij} + \eta_j + \varepsilon_i \quad [4a]$$

Model 4a will assess the probability, $\pi = ln\left(\frac{p}{1-p_{ji}}\right)$, of testing attendance for individual i in household j, where β_1 is the main effect for testing time (reference = Time 1); β_2 is the main effect for Financial Incentives (reference = lottery condition); β_3 is the main effect for Messaging (reference = personal); β_4 is the interaction between testing time and Financial Incentives; β_5 is the interaction between testing time and Messaging; and η_j is the random intercept for each household.

$$\pi = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij} + \beta_3 x_{ij} + \beta_4 x_{ij} + \beta_5 x_{ij} + \beta_6 x_{ij} + \beta_7 x_{ij} + \eta_j + \varepsilon_i \quad [4b]$$

Model 4b will assess the probability, $\pi = ln\left(\frac{p}{1-p_{ji}}\right)$, of testing attendance for individual i in household j, where β_1 is the main effect for testing time (reference = Time 1); β_2 through β_4 are the main effects for study arm (personal messaging and loss protection, family messaging and lottery, family messaging and loss protection), where personal messaging and lottery is the reference group; β_5 through β_7 are the interactions between study arm and testing time; and η_j is the random intercept for each household.

For Models 4a and 4b, we will use unrestricted random sampling to select 3,000 observations, 2,000 times, clustered by household to bootstrap 95% confidence intervals for probability differences. We will test differences in effect sizes for Model 4a (β_4 vs. β_5) and 4b (β_5 vs. β_6; β_5 vs. β_7; β_6 vs. β_7) using equality of regression coefficients tests.[6] We will also calculate the inverse of observed probabilities to derive the Number Needed to Intervene on (NNI), and calculate standard errors by taking the square root of $P * (1 - P)/N$.[7]

9.4.2 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will explore heterogeneity of treatment effects by using Model 2 to assess whether receptivity to study arm (e.g., personal messaging/loss protection) differs by significant social determinants of health identified in Hypotheses 1 through 5. To assess seroprevalence trends, we will use separate hierarchical models with a random household intercept to regress seropositivity status (yes vs. no), IgG value, and IgM value on testing time (Time 1 vs. Time 2).

9.4.3 SAFETY ANALYSES

The Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. We will establish a Data Safety and Monitoring Board (DSMB) in the first month of the project. The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the NIA Director to monitor

participant safety, evaluate the progress of the study, to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. We will establish a Data Safety and Monitoring Board (DSMB) in the first month of the project. The board will be composed of experts in behavioral economics, a physician with expertise in COVID-19, and a biostatistician. The DSMB is granted full power to recommend discontinuation of the study to the consolidated IRB, if safety concerns are found. A detailed Data and Safety Monitoring Plan will be submitted for IRB approval prior to the accrual of human subjects.

9.4.4 BASELINE DESCRIPTIVE STATISTICS

Intervention groups will be compared on baseline characteristics (e.g., demographics, laboratory measurements, behavioral characteristics) using descriptive statistics.

9.4.5 PLANNED INTERIM ANALYSES

There will be no interim analysis on the primary outcome. However, we will look at demographic characteristics of participants after 1 week of testing to determine stratification thresholds.

9.4.6 SUB-GROUP ANALYSES

All individuals meeting the study inclusion criteria will participate in the study. We will not under sample or oversample women and/or members of minority racial and ethnic groups, so we expect to enroll them in proportion to their population prevalence. We will have access to the sex/gender and race/ethnicity of participants and will conduct analyses to investigate any differences between groups. This project aims to evaluate the effectiveness of risk-based messaging and incentives that promote repeated testing for SARS-CoV-2 antibodies, as well as to understand social and behavioral determinants of COVID-19 testing and variations within sub-groups of this population.

9.4.7 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Not applicable

9.4.8 EXPLORATORY ANALYSES

Not applicable

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

Study participants will be recruited via phone by a culturally competent, bilingual research coordinator from our third party call center, The Henne Group (https://www.thehennegroup.com/). Consent for participating in the study will be a two-part process. First, participants will be asked if they would like to

participate in a survey about COVID-19. Participants who provide verbal consent for the survey will complete the baseline survey. After the baseline survey is completed, we will ask if the participant is interested in participating in testing. At the time of the test appointment, the study coordinator will check in each family member using their unique study ID. The coordinator will then conduct the informed consent process with participants in their preferred language.

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Each participant will sign a paper form (children 5-13 will sign the assent form; minors 14-17 and adults 18 and over will sign the consent form) and the CRC will take a photo of the forms and upload into the participant's REDCap record using the study iPad. Participants will be given the paper forms for their personal records. All participants will also sign the California Bill of Rights; AltaMed patients will be required to sign HIPAA authorization.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

A photo of the signed informed consent and assent forms will be uploaded into the participant's REDCap record using the study iPad. All study participants will receive a copy of the signed and dated consent document. The name of the CRC who consented the participants will be included in the participant record.

If a consent document is revised due to changes in study procedures, subjects who were enrolled prior to the change, but are affected by the change, will be informed of the changes and will sign the amended consent document. If a consent document is revised due to changes in the risks or safety of the study, all active participants must sign the revised consent. Informed consent will only occur at one time point (first test). If a minor turns 18 prior to the second test, we will re-consent them as an adult.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

Although we do not anticipate this happening, this study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

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

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (ie, significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, Food and Drug Administration (FDA), or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor or funding agency, representatives of the Institutional Review Board (IRB), regulatory agencies or representatives from companies or organizations supplying the product, may inspect all documents and records required to be maintained by the investigator. The study site will permit access to such records.

The study participant's contact information will be securely stored within the participant's REDCap record for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor/funding agency requirements.

All test results and survey data will be de-identified and the research team will never have access to the identifying information. Only AltaMed study personnel will have access to identifiers, and these will be stored in a secure location and destroyed after the study ends. Disclosure of survey responses or test results is highly unlikely. Data will be recorded with SSL protected web sites to a data warehouse, and transferred over secure network protocol. Data will be kept in encrypted files on a secure research computing cloud at USC Schaeffer Center facilities.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies
It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Per NIH, all study data and documentation will be retained for 3 years after study end.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Site Monitor**
Jason Doctor, PhD	*Mika Kadono, PhD*
University of Southern California	*AltaMed Institute for Health Equity*
635 Downey Way, Los Angeles, CA 90089-7273	*2035 Camfield Avenue, Commerce, CA 90040*
213.821.8142	*707.540.3435*

jdoctor@usc.edu	mkadono@altamed.org

See MOP for detailed list of study team roles and responsibilities of those involved in the conduct, management, or oversight of the trial.

10.1.6 SAFETY OVERSIGHT

The Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. We will establish a Data Safety and Monitoring Board (DSMB) in the first month of the project. The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the NIA Director to monitor participant safety, evaluate the progress of the study, to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. We will establish a Data Safety and Monitoring Board (DSMB) in the first month of the project. The board will be composed of experts in behavioral economics, a physician with expertise in COVID-19, and a biostatistician. The DSMB is granted full power to recommend discontinuation of the study to the consolidated IRB, if safety concerns are found. A detailed Data and Safety Monitoring Plan will be submitted for IRB approval prior to the accrual of human subjects. The DSMB will meet twice annually over the 2 year study timeframe. The meetings will occur by teleconference call to review study progress, data quality, and participant safety. The DSMB will provide its input to <specify the study sponsor/National Institutes of Health staff/other.

10.1.7 CLINICAL MONITORING

The purpose of the internal site monitoring is to ensure that the study processes are following proper study protocols and safety procedures, and there is proper and consistent quality control documentation at the AltaMed clinic study site, located at 2035 Camfield Avenue, Commerce, CA 90040 (the site). The on-site coordinator for AltaMed will monitor the site on a continuous basis through the duration of the study; the site monitor (off-site) will visit the site once per month.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

We will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. All sites will follow a common quality management plan. See details in the Manual of Procedures.

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Source documents and the electronic data --- All data will be captured in REDCap. To ensure accuracy site staff will compare a representative sample of source data against the database, targeting key data points in that review.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

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

All source documents will be entered and maintained in REDCap in a consistent manner to ensure accurate interpretation of data. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

10.1.9.2 STUDY RECORDS RETENTION

Per NIH policy, study data and documentation will be retained for 3 years after study end.

10.1.10 PROTOCOL DEVIATIONS

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

These practices are consistent with ICH GCP:

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

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 2 working days of identification of the protocol deviation. All deviations will be addressed in REDCap and reported to NIA Program Official. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing

and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

Our Resource Sharing plan is committed to the ideals of collaborative research, and as such, will adhere to the National Institutes of Health (NIH) policy on rigor and reproducibility and data and resource sharing. Oversight of the data and resource sharing will be conducted by Dr. Jason Doctor, PI of the proposed Supplement.

Study data will be maintained on a HIPAA compliant server where PI and Co-Investigators will have full access. All members of the investigative team are to share access to the data generated by the study for the purpose of preparing scientific presentations and manuscripts. The project manager will prepare and make available meeting minutes from all study meetings through Box, a secured access server extensively used by researchers at Schaeffer Center for Health Policy and Economics for collaborative projects. We will use data repositories such as github to post analysis code and data.

All data and resources generated through this project will be available for replication on a website or repository hosted on the Schaeffer research cloud. This will include a study protocol (with detailed information on recruitment, randomization, and workflow specifications), analytical codes, and any other study specific resources necessary to facilitate replication. The PI will share with the scientific community the analytical code produced as part of this project in a timely manner, and no later than the online publication date of any publications. To the extent allowed by scientific journals we will make the publications available as preprints or working papers. We will present preliminary findings at scientific conferences.

Data will be a HIPAA-compliant, limited data set. Prior to sharing of data, data use agreements will be executed and data will only be made accessible to key project staff. The data use agreement will include language requiring the user(s) to certify that no attempt will be made to reidentify participants from de-identified data. We will obtain consent to share de-identified primary data to the scientific community. These data will be available post publication of results to the network and broader scientific community. All project personnel handling study data will be certified by the Collaborative IRB Training Initiative (CITI) program, which consists of courses in the Protection of Human Research Subjects for Biomedical Research and added to the study IRB. These measures should be effective in minimizing breaches of confidentiality.

10.1.12 CONFLICT OF INTEREST POLICY

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

10.2 ADDITIONAL CONSIDERATIONS

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IDE	Investigational Device Exemption
IRB	Institutional Review Board
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

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

Version	Date	Description of Change	Brief Rationale

11 REFERENCES

1. Website. Accessed August 6, 2020. Food, U. S., Drug Administration, and Others. 2020. “EUA Authorized Serology Test Performance.” *https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance*.
2. Website. Accessed August 6, 2020. Food, U. S., Drug Administration, and Others. 2020. “EUA Authorized Serology Test Performance.” *https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance*.
3. Bajis S, Dore GJ, Hajarizadeh B, Cunningham EB, Maher L, Grebely J. Interventions to enhance testing, linkage to care and treatment uptake for hepatitis C virus infection among people who inject drugs: A systematic review. Int J Drug Policy. 2017;47:34-46.
4. Meeker D, Thompson C, Strylewicz G, Knight TK, Doctor JN. Use of Insurance Against a Small Loss as an Incentive Strategy. Decis Anal. 2015;12(3):122-129.
5. Meeker D, Knight T, Childress, P, Aliyev E, Doctor JN. Combining a lottery incentive with protection against losing the lottery improves exercise adherence. Behavioral Science & Policy, Volume 7 Issue 1, 2021.
6. Paternoster, R., Brame, R., Mazerolle, P. & Piquero, A. Using the correct statistical test for the equality of regression coefficients. Criminology 36, 859–866 (1998).
7. Altman, D. G. & Andersen, P. K. Calculating the number needed to treat for trials where the outcome is time to an event. BMJ 319, 1492–1495 (1999).