Study Title: Community Collaboration to Combat COVID-19 (C-FORWARD)

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**JHM IRB - eForm A – Protocol**

## 1. Abstract

a. Provide no more than a one-page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.

As with any rapidly changing viral outbreak, data in the SARS-COV-2 or COVID-19 pandemic is emerging daily, and many critical questions remain unanswered. For example, there is incomplete information on the true population burden of infection and long-term clinical consequences. Information on critical infectious disease transmission parameters remains unclear. Moreover, we do not understand the risks associated with the dynamics of transmission within the home, shelter, or other residential community setting. While clinical investigations of patients infected with COVID-19 can provide important information on individual level disease outcomes, population-based investigation is critical to understanding the 1) true population burden of disease; 2) access to and uptake of SARS CoV-2 testing; 3) transmission dynamics including the role of asymptomatic infections; and importantly the 4) short- and long-term social, economic and health consequences of the COVID-19 and associated control measures among communities that are most vulnerable. We propose to recruit a population-based sample in Baltimore City and randomize to different testing modalities in order to better understand the optimal modality for SARS-CoV-2 testing as well as the burden, transmission dynamics, clinical, social and economic consequences of COVID-19.

2. **Objectives** (include all primary and secondary objectives)

Enroll a population-based sample in Baltimore City to determine multilevel (socioeconomic, behavioral) barriers and facilitators to SARS-CoV-2 testing and prevalence and incidence of SARS-CoV-2.

1. Determine multilevel (socioeconomic, behavioral) barriers and facilitators to SARS-CoV-2 testing using a population representative sample of households in Baltimore, MD
2. Measure the prevalence of SARS-CoV-2 infection within a representative sample of Baltimore City
3. Define the optimal SARS-CoV-2 testing modality for maximizing testing acceptance, uptake and timeliness of providing results through a cluster-randomized comparative effectiveness trial
4. Determine the incidence of SARS-CoV-2 infection and associated risk factors including socioeconomic status
5. Evaluate the impact of testing modality and receipt of positive results on subsequent testing behavior and other behavioral, economic and clinical outcomes
6. Develop a data and specimen repository that will serve as a resource for the investigation and analysis of downstream research questions specific to the transmission of SARS-CoV-2, the clinical course of COVID-19, the development of preventive strategies and basic biologic and immunologic questions associated with SARS-CoV-2.

**3. Background** (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

The novel Severe Acute Respiratory Syndrome (SARS) Coronavirus 2019 (SARS-CoV-2 or COVID-19) emerged as a new viral infection in December 2019. Now a global pandemic, COVID-19 has presently sickened more than one million Americans in just three months with more than 50,000 deaths as of April 27, 2020. COVID-19 presents as a mild dry cough with or without fever and sore throat in the majority of people, yet progression to acute respiratory distress syndrome is possible but the symptom profile appears to be evolving. Initially, data emerging from China suggested the virus had the greatest morbidity and mortality in populations over the age of 70, however, recent data suggest that over 40% of individuals ill enough to require hospitalization are under the age of 50. As with prior coronavirus episodes, wide clinical variation from asymptomatic carriage to acute respiratory distress is unfolding. As with any rapidly changing viral outbreak, data is emerging daily, and little is known about duration of transmissibility, risk of transmission from asymptomatic carriers, environmental contamination and the dynamics of transmission within the home, shelter, or other residential community setting. Further, the long term sequelae of COVID-19 survivors, including their long-term immunity, lung function and other clinical sequala as well as the potential for re-infection is unknown.

Effective control requires changes in human behavior including reducing mobility, adoption of non-pharmaceutical interventions including masking and social distancing and testing and isolation of those infected or suspected to be infected. However, there are multilevel barriers to optimal testing in the population; these barriers are complex, dynamic and recursive (Figure 1).

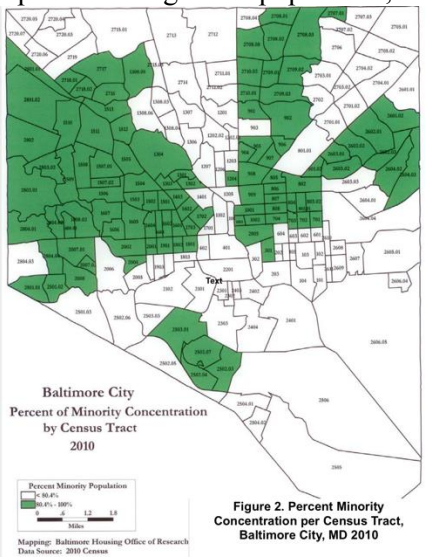
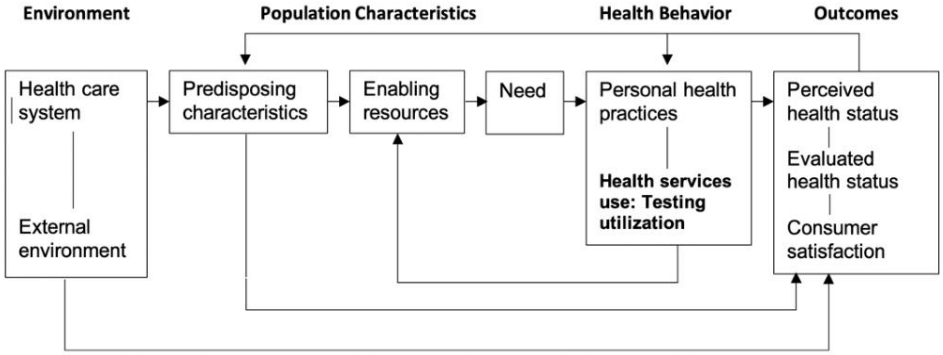



Figure 2. Percent Minority Concentration per Census Tract, Baltimore City, MD 2010

The framework portrays these multilevel determinants including the environment, population characteristics, and health behaviors that impact testing utilization and ultimately, health outcomes, including feedback loops indicating that downstream factors may negatively or positively reinforce upstream factors. The framework posits that there are environmental/health care system factors (e.g., testing supplies) and population predisposing, enabling, and need factors, all of which influence testing utilization and subsequent health outcomes. Predisposing factors include sociodemographic and other behavioral characteristics (employment and income). Enabling resources (or lack of) may include factors such as transportation access (e.g., public, personal), concentrated areas of poverty, and testing access (i.e., testing deserts). Need factors include general concerns about the pandemic and personal risk for infection.

**Figure 1. Conceptual Framework of SARS-CoV-2 testing utilization based on Behavioral Model of Access to Care.**




*Health and healthcare inequities will exacerbate poor testing access.* Latinx and Blacks are almost three and two times, respectively, more likely to be uninsured compared to non-Latinx whites. Blacks of all ages are also more likely to report not being able to see a doctor in the past year because of cost, which has direct implications for testing. In addition, longstanding issues of institutional (i.e., medical, research, public health) racism, mistrust and distrust, language barriers, and the cost of missing work all decrease the likelihood of testing among these subgroups. Blacks also experience higher rates of chronic conditions at earlier ages and at higher death rates, placing them at increased risk for COVID-19 illness severity and mortality and limiting their ability to seek testing. Racism, stigma, and systemic inequities at multiple levels, including healthcare systems, undermine prevention efforts, increase levels of chronic and toxic stress, and ultimately, sustain these inequities.

Community-based studies will be critical for understanding disparities that underly testing access and uptake. The proposed study will be able to define the optimal testing modality in order to maximize testing acceptance, uptake and timeliness of results. In Baltimore City currently, few sites offer testing to patients without symptoms and most still require both a state-level identification and a medical order prior to testing. Efforts to penetrate testing deserts often translate into weekly or monthly "pop-up" testing sites that are highly unpredictable for community members. Clinics dedicated to low-income residents have signs declaring limited capacity with testing offered "while supplies last". Our intervention will seek to overcome these multi-faceted barriers.

Beyond increasing our understanding of testing, this study will help to characterize the total spectrum of SARS-CoV-2 infection. COVID-19 is associated with a wide range of symptoms as well as spectrum of clinical illness. Little is known among patients who, ultimately, develop evidence of antibody demonstrating history of infection, yet who do not progress to hospitalization or Acute Respiratory Distress Syndrome (ARDS). For patients who do develop symptoms severe enough to warrant hospitalization, clinical evaluation includes multiple measures of inflammation – IL-6, LDH, ESR, CRP, CBC with differential. Additionally, clinical evaluation includes liver function testing and coagulopathy with D-Dimer. We seek to explore the extent of dysregulation among these parameters in individuals whose symptom spectrum is either prior to or does not lead to acute hospitalization.

Moreover, this study will provide critical information on community and specifically household transmission of SARS-CoV-2. Household transmission of both viral and bacterial pathogens is common and well established. In the outbreaks of SARS, the Middle Eastern Respiratory Syndrome (MERS) and Avian Influenza (H1N1), household transmission ranged between 5% in MERS, 6.2% in SARS, and 81% in H1N1. The transmissibility of COVID-19 is estimated to be higher than both MERS and SARS, yet lower than H1N1. Sub-clinical transmission within

households has also been identified between MERS index cases and household contacts. With most of the household/residential studies, it is unclear whether direct contact with the index case or contact with a fomite within the residence is the source of transmission.

## 4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

**Study design**

Population-based sample of households within Baltimore city with randomization to SARS-CoV-2 testing modality and follow-up for up to 6 months.

The overall study is divided into two Phases: Phase I will include a survey to meet objective 1 and Phase II will include randomization and follow-up to achieve objectives 2 through 6.

**a. Phase I - Survey**

**I. Sampling**

The target population will include English- and Spanish-speaking families residing in Baltimore City households (N=238,427). The sample size goal for Phase I is 1,386 households (or 0.44% of households). To achieve this sample, the main recruitment method will be a stratified household sampling frame with recruitment by mail, telephone and/or online methods. The sampling frame information has been obtained from two main sources. From the Department of Housing and Community Development in Baltimore City, we obtained a list of all households in Baltimore City including information on vacant status, residential vs. business status and single vs. multi-unit dwellings. The second source will be telephone and email information obtained from direct mailing and marketing vendors (e.g. Valassis, Lexis Nexus, Dataman), in the form of a purchased address, telephone and/or online contact lists.

We will use a multi-stage approach with 1) selection of 105 of 653 census block groups (CBGs) with probabilities proportional to the estimated number of occupied households selected from 9 strata of CBGs defined by socioeconomic status and race/ethnicity with oversampling of CBGs with harder-to-reach populations (e.g., Latinos/x, low-income whites); 2) selection of residential addresses within each of the strata via non-linear optimization; and finally, 3) screening of individuals selected for eligibility (e.g., occupied vs. not, English/Spanish speaking).

**II. Household Index Recruitment**

Recruitment will be multi-modal including a doorhanger, mailing, telephone and/or online methods with up to 10 attempts for every household. The recruitment will begin with a doorhanger (see DOORHANGER) for selected households followed by a postcard (see POSTCARD), both of which will include study contact information.

A lead letter will be mailed to each selected household that includes study contact information, and an informed consent form (see SURVEY CONSENT FORM).

For households with phone numbers, text messages and telephone calls (see details below) will be made to reach an adult willing to participate. For households without these contact methods, an additional postcard will be sent to the household.

A week after the postcard is mailed, a trained research assistant will contact the potential household, introduce themselves, give a key engagement message about the study, and ask first if they are speaking with a person who is 18 years or older. If yes, then the research assistant will ask if they would be willing to answer a few questions which will assess study eligibility. If the individual is not 18 years or older, the research assistant will ask to speak to an adult member of the household or ask for a good time to call back when an adult member will be home. If the individual indicates that they are not interested or do not want to provide any information, the research assistant will thank the individual for their time. The research assistant will make a minimum of 7 attempts to reach an adult member of the household unless they receive a refusal for the household to participate. For those households for which we also or only have an email address, similarly, a trained research assistant will send an email with an introduction, key engagement message and provide a phone number and email to call or email for more information, respectively. A standard study telephone number, 1-855-6C4-WARD number and email, CFORWARD@jhu.edu will be provided on study materials to streamline communication. In addition, each individual will be given phone numbers of the PI and the IRB office to contact if they have additional questions or concerns.

At this stage, the goal is to enroll a single adult in the household. Once contacted and consented by a trained study team member, this participant will be instructed to complete a survey in phase I of the study. If the adult household index agrees to future contact for COVID-19 research, the index will be contacted again for phase II of the study, which includes enrollment of household members (if willing) and testing for SARS-CoV-2.

**1. Informed consent**

Oral informed consent will be obtained from an adult in the household (18 years or older). There will be no specific selection within the household. Whoever is reached first / whoever is willing will be asked to participate in this phase.

Oral consent procedures will be conducted by a study team member as follows. The study team member will review the informed oral consent document with the potential participant over the phone. If the participant would like a copy of the oral consent, a copy can be emailed or texted immediately with a link to REDCap or can be mailed for a discussion at a later date. No electronic signature is required for this part of the consent but they will be asked to provide consent for contact for future studies (e.g., Phase II). The study team member will electronically sign the consent form in REDCap to reflect oral consent to both 1) participation in Phase I; and 2) contact for future studies (Phase II). The household index will be given phone numbers of the PI and the IRB office to contact if they have additional questions or concerns.

**2. Survey (mail-in/phone/online)**

***Administration:*** There will be three options for administering the Phase I survey that will be offered to participants. The first and preferred option will be a survey that is administered by an interviewer via telephone and entered directly into a REDCap database. The second option will be to provide a link to an online secure survey. The third option will be a hard-copy mail-in survey. It is anticipated that the household survey will take 30 minutes.

***Survey:*** The survey will include questions at the household and individual-levels. The household-level will capture information on the household: 1) type of home including number of bedrooms and bathrooms; 2) detailed inventory on all household members

including age (grade for children under 18), sex, race and employment; 3) household experiences with COVID-19 symptoms, testing, treatment and hospitalization. The individual-level will include 1) demographics, 2) individual COVID-19 symptoms, testing and treatment experience (chronic health condition, previous covid-19 testing, treatment and hospitalization), 3) adoption of prevention behaviors, 4) comorbidities and health care access 5) coronavirus impact and pandemic stress, 6) mental health, 7) social connectedness, 8) substance use 9) knowledge and attitudes towards COVID-19.

***Contact information:*** We will also collect preferred method of contact in the event that the survey is interrupted for any reason and another appointment to complete the survey is necessary as well as to provide renumeration and for contacting those participants providing informed consent for future studies.

Co-enrollment in another study is allowed in this protocol.

**b. Phase II**

**I. Enrollment and informed consent**

All index household participants will be eligible to enroll in Phase II. The research assistant will also ask for permission to contact any other adult household member (identified in the household inventory) to see if they would be interested and willing to participate in Phase II. If yes, the research assistant will collect contact information and document the permission to contact. If no, the research assistant will let the index participant know that other adult household members can be referred into the study and can contact the study at any time using the methods provided (i.e. website, phone number, text, email).

Phase II enrollment for the household index will either continue immediately after completion of Phase I (if the participant is willing) or at a later mutually agreed upon day/time if the participant prefers to be contacted later. If continuing immediately, the informed consent for Phase II will be provided to the household member participant with a link to REDCap (online via text or email). If the index participant is interested in enrolling in Phase II, but does not have access to the internet, a hard copy of the consent will be mailed and enrollment in Phase II will take place on a later date. After receipt of the consent form, the research assistant will review the consent form with the participant. Oral informed consent for Phase II will be obtained from the participant and comprehension of consent assessed. The study team member will electronically sign the consent form for Phase II in REDCap to reflect oral consent to both 1) participation in Phase II; 2) consent for storage of biospecimens; 3) consent for genetic studies.

**II. Randomization:**

Once any adult household member enrolls in Phase II, randomization of the household to one of the three testing modalities will occur by the following approach. We will use an individual-level stratified blocked randomization approach that considers the importance of geographic access to testing sites (such as access for arm I – standard of care testing sites) and individual level information provided in Phase I including race/ethnicity (non-Hispanic White including Non-Hispanic Other, non-Hispanic Black, Hispanic/Latinx). The CBGs (n=105) selected as a part of the sampling strategy will be classified into 12 strata according to geography. Allocation sequences will be generated

per stratum (n=12) per race/ethnicity/poverty (n=8) for a total of 96 strata. The sequences will be integrated into REDCap using varying blocks sizes of 3 and 6 and households which will be allocated at a 1:1:1 ratio to one the three testing modalities. The randomization will apply to all members of the household who participate in Phase II, i.e. all household members will have the same randomization allocation.

## III. Recruitment of household members

### 1. Consent/Assent for household members

The same consent form shared with the household index can be shared with all other household members who are 18 years of age or older. The same processes followed in Phase I for obtaining informed consent will be followed. Phase II will consist of a survey for other household member participants (see below Surveys for household members), and for all household participants, testing according to household randomization assignment (see Study Arms), the collection of host genetics and the storage of biospecimens. In addition, each participant will be given phone numbers of the PI and the IRB office to contact if they have additional questions or concerns.

During the inventory started in Phase I and completed in Phase II we will assess the following details for each household member between the ages of 12 to 17 (prior to January 3, 2022) (i.e. child): a) grade; b) age; c) the name of parent / legal guardian and d) whether or not the parent / legal guardian is within this household. After January 3, 2022, we will assess these additional details only for each household member between the ages 16-17. This is documented within REDCap. This information will used to determine the parental/ legal guardian consent and assent process for the child. We will use the following strategy:

a. For children from 9th grade on, assent will be obtained by via presentation of the parental permission consent script.

*All consent/assent form documents will be combined by the study team member and uploaded into one document into EPIC.*

### 2. Surveys for household members

All household members who enroll will be asked to complete individual surveys either by phone or online. The survey will be similar to that administered to the household index and will include questions on 1) demographics, 2) individual COVID-19 symptoms, testing and treatment experience, 3) adoption of prevention behaviors 4) comorbidities and health care access 5) coronavirus impact and pandemic stress 6) mental health 7) social connectedness 8) substance use 9) knowledge and attitudes towards COVID-19. Separate surveys will be used for household members 12-17 years of age (prior to January 3, 2022) and only those aged 16-17, as well as 18 years of age and older after January 3, 2022.

## IV. Study Arms (Testing Modalities)

Households will be randomized to one of three study arms (see randomization). A description of each study arm is provided below and in **Table 1**.

## 1. Arm 1

***Fixed site SOC testing.*** This arm includes all three Johns Hopkins (JHMI) ambulatory outdoor testing sites across Baltimore City. Each site represents a traditional appointment-based scheduling system. Participants will be given a choice of 1 of 3 outdoor testing locations based on their preferences. Study staff will make an appointment for testing based on testing availability and participant schedule.

Prior to June 30, 2021 there were three JHMI testing sites available.

After June 30, 2021, only two JHMI testing sites: (i.e., Johns Hopkin Bayview Medical Center Testing Tent and Johns Hopkins School of Nursing) are available as testing sites. The Johns Hopkins Greenspring Station tent was closed as of June 30, 2021.

The laboratory tests to be conducted at the fixed site (Arm 1) by household member(s) are as follows:

***Nasopharyngeal (NP), Nasal, Middle Turbinate (MT) and/or Oropharyngeal (OP).*** The NP, MT and/or OP swabs, based on availability, will be collected through standard clinical care, as described above. All staff will be trained using the same techniques for NP, MT and OP swabs as the JHMI testing sites. If either the NP, MT or OP sites are positive, those results will be communicated with the patient. This test result will be provided to the patient.

***Blood specimens.*** Serum for antibody will be collected. Clinical evaluation includes multiple measures of inflammation – IL-6, LDH, ESR, CRP, CBC with differential. Additionally, liver function testing and coagulopathy with D-Dimer.

***Plasma and Peripheral Blood Mononuclear Cells (PBMC)***. Blood will be collected for storage of plasma and PBMCs for storage in the Johns Hopkins Biorepository (JHBR). All participants will have the option to opt-out of this collection in the oral informed consent document. This blood will be used for the development of future, yet as unplanned, studies. Our team has an extensive history of following JHBR policy/procedures for the processing and storage of specimens with this team. Standard chain of custody and operating procedures will be followed.

***Serum host genomics.*** Blood will be collected for storage of host genetic testing. Participants will have an option to opt-out of this collection as part of the future studies in the written informed consent document. Standard chain of custody and operating procedures will be followed.

***Saliva PCR/Antibody/Antigen testing.*** We will collect 5-10mL of saliva for validation studies as a possible modality for viral RNA sampling and antibody testing. This testing is currently for research purposes only and the result will not be communicated with the patient until the laboratory has validated and approved this mode of PCR testing and/or antibody/antigen testing.

## 2. Arm 2

***Community-based, mobile van testing.*** This arm offers the convenience of highly accessible testing and with the flexibility of no fixed appointment time. Each of the 12 geographic strata (see randomization) will have a single, centrally located testing site within the area, providing similar geographic access across households. The testing

location will be published on the study website and social media so that participants can visit the location at a time convenient to them.

The laboratory tests to be conducted at the mobile van (Arm 2) by the household member(s) are as follows:

***Nasopharyngeal (NP), Nasal, Middle Turbinate (MT) and/or Oropharyngeal (OP).*** The NP, MT and/or OP swabs, based on availability, will be collected through standard clinical care, as described above. All staff will be trained using the same techniques for NP, MT and OP swabs as the JHMI testing sites. If either the NP, MT or OP sites are positive, those results will be communicated with the patient. This test result will be provided to the patient.

***Blood specimens.*** Serum for antibody will be collected. Clinical evaluation includes multiple measures of inflammation – IL-6, LDH, ESR, CRP, CBC with differential. Additionally, liver function testing and coagulopathy with D-Dimer.

***Plasma and Peripheral Blood Mononuclear Cells (PBMC)***. Blood will be collected for storage of plasma and PBMCs for storage in the Johns Hopkins Biorepository (JHBR). All participants will have the option to opt-out of this collection in the oral informed consent document. This blood will be used for the development of future, yet as unplanned, studies. Our team has an extensive history of following JHBR policy/procedures for the processing and storage of specimens with this team. Standard chain of custody and operating procedures will be followed.

***Serum host genomics.*** Blood will be collected for storage of host genetic testing. Participants will have an option to opt-out of this collection as part of the future studies in the written informed consent document. Standard chain of custody and operating procedures will be followed.

***Saliva PCR/Antibody/Antigen testing.*** We will collect 5-10mL of saliva for validation studies as a possible modality for viral RNA sampling and antibody testing. This testing is currently for research purposes only and the result will not be communicated with the patient until the laboratory has validated and approved this mode of PCR testing and/or antibody/antigen testing.

**3. Arm 3**

***Self-collected, home-based testing.*** Individuals will receive a home-based testing kit delivered via courier service as soon as the randomization of the household is complete. Prior to January 3, 2022, return of the kit was also via courier service. After January 3, 2022, the PCR kit will include provisions for the shipping of samples directly to a company called, Everlywell, via UPS dropbox and/or fixed UPS location. The saliva kit will be mailed via the same method. Appropriate biohazard precautions are included. The home-based testing kit will include an anterior nares (AN) specimen and saliva collection device for SARS-CoV-2 RT-PCR, and for those enrolling prior to December 10, 2021, a liquid blood collection system. Each of the testing components of this kit will include FDA Emergency Use Authorization approved collection methods. Easy to use instructions with options to view pre-recorded videos and/or virtual ‘on demand’ coaching sessions with members of the study team via a HIPAA-secure Zoom session will be available.

The home-based self-collection kit tests to be completed in (Arm 3) by the household member(s) are as follows:

***PCR Nasal swab.*** The nucleic acid test (PCR) will be performed by eligible individuals enrolled in the household. The PCR test is very sensitive, which will allow for detection of a SARS-CoV-2 genetic material. The nasal swab included has all supplies needed for collection and return of the self-administered test.

***Saliva Sponge testing.*** The sponge collection tube will be performed by the eligible individual enrolled in the household. This will allow for the rapid collection of saliva to be collected, placed in a tube. The device is shipped in a clinical container that includes all supplies needed for collection and return of the self-administered test.

**For those enrolling prior to December 10, 2021:** ***Tasso SST blood collection device.*** This device will be performed by the household on eligible individuals enrolled, which will allow a small liquid blood sample to be collected and mailed back to the lab for analysis. The kit includes all supplies needed for collection and return of the self-administered test.

In order to reduce the variability of health system-associated delays in testing and results counseling, all three arms will include these four components: a) scheduling without a medical order; b) testing regardless of exposure risk or symptoms; c) processing of specimens by the same lab; and d) results communication with counseling for positive and negative test results (see **Table 1**).

**Table 1. Summary of Testing Modalities**

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

**VI**. **Healthcare worker and research staff safety**: Infection control procedures for face-to-face visits for those in Arm 1 and 2 are identified below in the risks section below. Staff collecting any specimen and/or having face-to-face contact with study participants will either be in a positive-air purifying respirator (PAPR) or fit-tested N-95 with appropriate eye coverage. The procedures here are designed to limit contact time, maximize protection and

optimize PPE use for the given types of contact. Given that individuals in this study will include PUI and confirmed cases, all individuals will be considered infectious and appropriate precautions taken. Infection control procedures for Arm 3 are in the risks section below.

Each testing modality has similar goals: 1) verification of symptoms and clinical presentation; 2) standardized COVID-19 education; 3) laboratory testing; 4) contact identification.

***Verification of Symptoms and Clinical Presentation:*** For arms 1 and 2, a staff member will meet the participants from a single household at a JHMI testing site or community based mobile van and will verify the previously reported symptoms (from the online or phone survey) to ensure no changes. Staff will complete an update of this form to document this verification and determine if any symptom has changed from the phone-based/online interview. If anyone from the household reports any symptoms at this screen, the research assistants will complete a health department "Person Under Investigation, PUI" form for all suspected SARS-CoV-2 cases – (i.e., all symptomatic participants without confirmed infection). The PUI form will be faxed to the Maryland Department of Health. Additionally, if anyone from the household reports symptoms at a mobile van visit, the entire household will be immediately referred to one of the testing tents for completion of their visit. Symptom screening will follow the standardized clinical protocol developed by The Johns Hopkins Hospital Epidemiology and Infection Control team for ambulatory triage. Patients whose symptoms have progressed to include worsening shortness of breath, or low oxygen saturation < 93% or other CDC recommended referral criteria will be immediately referred to the emergency department or, 911, as needed.

For Arm 3**,** home based collection kits sent to a household will have a sticker on the box with a number to text or call to indicate to the lab team of kit arrival. Once receipt of the home test kit is confirmed, the participant will be sent an online survey to self-report symptoms to ensure no changes. Research staff will compare this form to the original to determine if any symptom has changed from the phone-based/online interview. If anyone from the household reports any symptoms at this screen, the research assistants will complete a health department "Person Under Investigation, PUI" form for all suspected SARS-CoV-2 cases – (i.e., all symptomatic participants without confirmed infection). The PUI form will be faxed to the Maryland Department of Health.

***Education:*** A Standardized SARS-CoV-2 handout will be mailed to all participants with the questionnaire and informed consent documents in arm 3 only, while Arm 1 and 2 participants will receive this handout in person. This handout includes basic information about the infection, symptoms, how to prevent infection and when to contact the study team should symptoms arise. Additional information about severe symptoms are also included and when to call 911 or present to the emergency department. We will re-iterate basic information during the visit and will be screening for symptoms that indicate the need for medical referral as noted above.

***Blood volume:*** To maintain our designation as a minimal risk research protocol, we are proposing the following designation of participants as "healthy volunteers" or "unhealthy volunteers" in the context of COVID-19. Blood volume for each test will be adjusted for the size and weight of the participant < 18 years of age. For these subjects, the amount drawn may not exceed the lesser of 50 milliliters or 3 milliliters per kg in an 8-week period and collection may not occur more frequently than 2 times per week. We will utilize the following definitions:

Healthy volunteers: 1) a participant who is an asymptomatic for COVID-19 regardless of their medical comorbidity profile with the exceptions noted below; or 2) a person who is 7 or more days from their last COVID-19 sign/symptom (i.e., convalescent) based on self-report of the date of symptom onset and resolution. The ***total blood volume*** over an 8-week period in the healthy volunteer sample ***will not exceed 550 milliliters***.

Unhealthy volunteers: 1) a symptomatic participant is an individual with self-report of active symptoms and those whose symptoms may have resolved in less than 7 days since symptom resolution; 2) self-report or medical record identification of anemia (defined as a hemoglobin level < 13 in men or < 11 in women); 3) medical diagnosis by which, in the opinion of the investigators, would classify a person as "unhealthy" for the purposes volume of the blood draw at a given visit. The ***total blood volume*** over an 8-week period in the unhealthy volunteer sample ***will not exceed 50 milliliters***.

**Background for choices of laboratory testing**: According to a review in the Annals of Internal Medicine (Cheng MP et al *Ann Intern Med* 2020), the most common laboratory features reported in patients with COVID-19 include decreased ***albumin*** (75.8% [95% CI, 30.5% to 100%]), elevated ***C-reactive protein*** (58.3% [CI, 21.8% to 94.7%]), elevated ***lactate dehydrogenase*** levels (57.0% [CI, 38.0% to 76.0%]), and ***lymphopenia*** (43.1% [CI, 18.9% to 67.3%]) (56). Other biomarkers include increased erythrocyte sedimentation rates, elevated ***aspartate aminotransferase***, ***alanine aminotransferase***, creatinine kinase levels, ***leukopenia***, ***leukocytosis***, and increased ***bilirubin*** and ***creatinine*** levels. No biomarker or combination of biomarkers currently exist that are sensitive or specific enough to establish a diagnosis of COVID-19, or to pragmatically predict its clinical course. We have selected the bolded biomarkers for inclusion here. Given that our household survey is a community sample, we hope to correlate mild to moderate symptoms with the presence or absence of these biomarkers. We will also be testing the virus on random positive SARS-CoV-2 samples for viral genome sequencing.

**VII. Specimen collection and Laboratory Testing Capacity**. Testing and biospecimen collection will be completed for participants ≥5 years of age enrolled into the study prior to January 3, 2022. After January 3, 2022, testing and biospecimen collection will be completed for participants > 16 years of age. For those randomized to the mobile van or fixed testing site, samples will be collected in person. Prior to December 10, 2021, each arm will collect an AN and saliva specimen for RT-PCR/antibody testing, as well as blood for antibody testing. After December 10, 2021, the self-collected home-based testing arm (Arm 3), will no longer collect a blood specimen for antibody testing. Additional testing will be completed at the in-person visit. For those randomized to home collection testing (Arm 3) only a Nasal PCR and saliva sample will be collected.

All RT-PCR testing will be performed at the Johns Hopkins Hospital by Dr. Mostafa and her team of clinical microbiologists using assays authorized by the FDA. Antibody testing will be performed by Johns Hopkins Clinical Immunology using assays authorized by the FDA. Processing for both tests will follow the clinical standard of care for patients at Johns Hopkins Hospital. The Johns Hopkins Biological Repository will handle all processing, storing, and testing services for stored specimens. Personal protective equipment, cleaning supply chain and staff protections are described in the Facilities and Environment and Human Subjects Research sections.

## VIII. Phase II: Follow-Up Visits

***Weekly Pulse Surveys:***

All participants enrolled in Phase II will be invited to participate in longitudinal follow-up to monitor symptoms and factors associated with additional testing uptake and timely completion. By either telephone call, text message, or an online link, participants will be asked to respond to weekly pulses. All household member participants will be asked to respond to these surveys and the household index member will be asked to report on all family members in case not all household members agree to participate. A questionnaire will ask about individual symptoms, symptom onset date, and severity. Additional questions will ask about any testing that was received outside of the study and any contacts with known COVID-19 cases either through personal knowledge or contact tracing. Symptoms will be classified into the following categories: major respiratory (e.g., shortness of breath), major systemic (e.g., chills, fever); major neurological (e.g., loss of smell), minor systemic (e.g., headache), minor respiratory (e.g., sore throat), minor gastrointestinal (e.g., diarrhea) and minor neurological (e.g., dizziness). Any report of new onset (past 7 days) major symptom or two minor symptoms classes will trigger an offer of repeat testing. Similarly, any report by a participant of either 1) close contact (defined as face-to-face contact within six feet and for more than 15 minutes) with a confirmed COVID-19 case; 2) a SARS-CoV-2 positive test result outside of the study of any household member; or 3) being contacted by the health department because of contact with a known COVID-19 case will be a trigger for an offer of testing. When an individual in a household is indicated for testing, all household members will be offered testing through their initially randomized modality.

***Monthly Telephone/Online-Based Visits (Month 2 – 5):***

This visit will occur by telephone or online.

*Survey (phone/online):* At monthly intervals, we will conduct follow-up surveys among participants (12 years of age or older) with multiple options for completion including phone or online for those enrolled prior to January 3rd, 2022. After January 3rd, 2022, only those 16 years of age that are enrolled will be followed using multiple options for completion of phone or online surveys. Both options will be available, and participants can choose different options at different visits. The follow-up questionnaire will be approximately 10-15 minutes for the household survey and 5 minutes for the individual survey.

*Follow-up household survey:* The household index member enrolled in Phase I will have completed a household survey. The follow-up household survey will capture new onset of symptoms in the prior month for any household members, experiences with testing and hospitalization and a brief assessment to assess impacts and changes within the prior one month on income, employment, healthcare access, distress and household adoption of preventive measures. Additionally, the household survey will capture any changes in household composition and/or contact information for participating household members.

*Individual survey*: All enrolled individuals (including the household index) will receive a brief survey regarding COVID-19 symptoms and clinical outcomes as well as a brief assessment of distress/mental health impacts of COVID-19 and adoption of prevention measures. New onset symptoms will result in an "interim" testing visit.

***Month 6 Visit:***

A final visit at month 6 will repeat the same process as the baseline enrollment visit. All participants will be asked to complete the final testing visit via the JHMI testing tent for

standard of care, fixed site testing of Arm 1 and Arm 2. Arm 3 participants will receive PCR, and saliva only, unless symptomatic, in which case additional labs and a participant referral to the JHMI testing site would be warranted.

***Interim Testing 'Visit':***

This visit is designed only for households where there is 1) a newly symptomatic individual; 2) someone who reports testing positive outside of the study at a weekly or monthly pulse; and 3) someone who reports wanting or needing a test because of a suspected exposure. Testing will only be completed for those determined to not require immediate emergency department referral via telephone interview using the JHMI ambulatory triage protocol. Household members will be provided with a choice of testing modality including the JHMI testing tents (Arm 1) or home-based testing (Arm 3) (identical to those described above). This testing 'visit' will be scheduled for all members of the household regardless of whether any other household members report symptoms or a positive test result.

During this interim assessment we have four main goals: 1) verification of symptoms and clinical presentation; 2) standardized COVID-19 education; 3) laboratory testing; 4) contact identification, as identified in the intake visit. Symptoms that meet the criteria for suspected coronavirus will trigger an additional series of questions about severity and scheduling for immediate testing (see below).

Similarly, those that report receiving a positive test outside of the study will be asked additional questions about where testing was received and time since positive test and will also be scheduled for testing. Those who report suspected exposure will be asked more details about this exposure and scheduled for a testing visit.

As appropriate, a PUI form and contact tracing log will be completed.

**Table 4. Phase I & II - Surveys and Follow-Up**

| Phase I & II - Surveys | Phase I | Weekly | Month 2-5 | Month 6 | Interim Testing Visit |
|---|---|---|---|---|---|
| **Household Index** | | | | | |
| Demographics | X | | X | X | X |
| COVID-19 Symptoms Testing, and Treatment Experience | X | X | X | | X |
| Adoption of Preventive Behaviors | X | | X | X | X |
| Comorbidities and Health Care Access | X | | X | X | X |
| COVID-19 Impact and Pandemic Stress | X | | X | X | X |
| Mental Health & Substance Use | X | | X | X | X |
| Knowledge and Attitudes Towards COVID-19 | X | | X | X | X |
| Catch Up for Missed Pulses | | | X | X | |
| Vaccine Perceptions (WK1) | | X | | | |
| Social Distancing (WK2) | | X | | | |
| COVID-19 Treatment Perceptions (WK3) | | X | | | |
| **Individual (12-17 & 18 and older)** | Phase II | | | | |
| Demographics | X | | X | X | X |

| | | | | | |
|---|---|---|---|---|---|
| COVID-19 Symptoms Testing, and Treatment Experience | X | X | X | | X |
| Adoption of Preventive Behaviors | X | | X | X | X |
| Comorbidities and Health Care Access | X | | X | X | X |
| COVID-19 Impact and Pandemic Stress | X | | X | X | X |
| Mental Health & Substance Use | X | | X | X | X |
| Knowledge and Attitudes Towards COVID-19 | X | | X | X | X |

***Communicating antibody results***: This is a rapidly evolving space. At present, we will plan to follow the clinical standard of care based on JHMI Clinical Immunology guidance. At a minimum this communication will include the following: 1) antibody status (positive or negative); 2) warning about the lack of certainty about prevention of re-infection; 3) guidance on discussing the result with their personal healthcare provider before changing any social distancing habits.

**Table 4b. Phase II - Testing and Follow-Up**

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

| | | | | | |
|---|---|---|---|---|---|
| Saliva Sponge | X | | | X | X |
| Tasso SST blood collection device (for only those enrolled prior to December 10, 2021) | X | | | X | X |
| Everlywell PCR Nasal Swab | X | | | X | X |

**IV. Contact Tracing:**

Anyone who tests positive by RT-PCR at any time during the study will be referred to the Baltimore City Health Department for contact tracing.

**X. Medical record linkage:**

All participants will be asked about hospitalizations and visits with health care providers at the baseline and follow-up visits. At baseline, participants will be asked to sign an authorization to request medical records to obtain access to medical records for diagnosis. Specifically, we will incorporate into the consent and in the medical records release the authority to obtain clinical information from the Maryland Health Information Exchange (Chesapeake Regional Information System for our Patients [CRISP]). The goal of this linkage will be to obtain information on COVID-19 testing outside of the study and health care visits and hospitalizations for COVID-19 as well as other related health conditions.

XI. In-depth Interviews:

We will further explore barriers and facilitators to COVID-19 testing by conducting an a telephone-based in-depth interview (IDI) with a subsample of Phase II participants in each testing arm. . IDIs will be conducted with 96 participants (N=32 per testing modality) to access acceptability of each modality, and general and modality-specific barriers and facilitators to testing. Participants will be purposively sampled from low-income CBGs for each modality based on testing completion (yes/no) and race/ethnicity (non-Hispanic Black, non-Hispanic White, and Latinx). Interviews will be conducted one month after a participant enrolls in Phase II and is assigned to a testing modality to allow time for testing and receipt of test results to occur. Interviews will explore testing concerns and/or barriers, accessibility of testing, acceptability of the assigned testing modality, and testing experience (if participant completed testing). Interviews with all participants will also solicit recommendations for improvements related to their respective testing modality.

**b.** If your study involves data/biospecimens from participants enrolled under other research studies with a written consent or under a waiver of consent, please list the IRB application numbers for those studies. Please note: Certificate of Confidentiality (CoC) protections applied to the data in source studies funded by NIH or CDC will extend to this new study if the funding was active in 2016. If this situation applies, Section 36, question 4 in the application will need to be answered "Yes" and "Hopkins Faculty" should be selected in question 7. No other documents are required. **N/A**

c. Study duration and number of study visits required of research participants.

Study duration: 6 months

Number of visits: Baseline + 11 follow-up visits (Baseline and 6-month visit -Follow-up visit 5) will include mail/phone/online and in person components whereas Follow-up visits 1-10 will also include mail/phone/online components.

Additional weekly contacts by phone/online for symptom reporting/testing updates

Number of study visits among IDI participants: Participant will be asked to complete one interview on the phone that will take approximately 1 hour.

**d.** Blinding, including justification for blinding or not blinding the trial, if applicable. **N/A**

**e.** Justification of why participants will not receive routine care or will have current therapy stopped. **N/A**

**f.** Justification for inclusion of a placebo or non-treatment group. **N/A**

**g.** Definition of treatment failure or participant removal criteria. **N/A**

**h.** Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely. **N/A**

5. **Inclusion/Exclusion Criteria**

For Phase I, eligibility for participation will include an English- or Spanish-speaking resident of the selected household located within Baltimore City. (see inclusion/exclusion criteria below) The first participant of the household (index) will need to be an adult member, 18 years or older who resides in that household more than four nights per week since March 1, 2020.

Inclusion criteria for Phase I

a. Selected address within Baltimore City
b. At least one member of the household ≥18 years of age who speaks English and/or Spanish
c. At least one member of the household provides informed consent
d. At least one member of the household psychologically fit to complete survey

Exclusion criteria for Phase I

a. Adult member of the household is under the influence of illicit substances, in the opinion of the phone interviewer
b. Residents of nursing homes, half-ways houses or shelters

Inclusion criteria for Phase II

All those enrolled in Phase I will be eligible for enrollment in Phase II. In addition to the household index enrolled in Phase I, all household members (defined as individuals that share kitchen/living space since March 1, 2020 and 5 years of age or older) will be eligible for participation in Phase II if enrolled prior to January 3rd, 2022. If enrolled after January 3rd, 2022, all household members are eligible (defined as individuals that share kitchen/living space since March 1, 2020 and are 16 years of age or older).

a. Reports primary residence within the sampled household
b. Provides informed consent
c. For adolescents (16 years of age or older), with assent.
d. Psychologically fit to complete the survey

Exclusion criteria for Phase II

a. Person providing informed consent is under the influence of illicit substances

6. **Drugs/ Substances/ Devices**

**a.** The rationale for choosing the drug and dose or for choosing the device to be used. **N/A**

**b.** Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed. **N/A**

**c.** Justification and safety information if non-FDA approved drugs without an IND will be administered. **N/A**

7. **Study Statistics**

a. Primary outcome variable.

Timely completion of SARS-CoV-2 viral testing and receipt of results; defined as receipt of test results within 5 days of randomization.

Our analysis will compare the effect of each of the two testing modalities (mobile van testing, home-based testing) and the SOC (fixed site testing) in analyses summarizing the proportion receiving results within 5 days at the cluster level.

b. Secondary outcome variables.

Prior history of SARS-CoV-2 antibody testing

Testing access when a test was indicated either because of symptoms or known contact with a SARS-CoV-2 case

Delays in testing from the onset of symptoms

Delays in receiving results after testing

Prevalence of current infection with SARS-COV2

Incidence of symptoms consistent with COVID-19

Incidence of new infection with SARS-COV2

Incidence of hospitalization for COVID-19

Incidence of re-infection

Mortality

Symptom duration and sequala in patients with known COVID-19 infection

Loss of employment by an adult member of the household due to COVID-19-related layoffs

Loss of housing (such as an eviction)

Report of food scarcity

c. Statistical plan including sample size justification and interim data analysis.

**Sample size justification**:

**Phase I:**

A population representative sample will reveal prior prevalence of prior SARS-CoV-2 testing based on households with oversampling of socially vulnerable subgroups in Baltimore City. Estimates suggest that anywhere from 5% to 15% of persons in Baltimore have ever received a SARS-CoV-2 viral test. We conservatively aim that at the time of the survey, 10% will have been tested at least once. Under a two-level cluster sampling strategy, the design-effect is dependent on n, or the average number of households within each selected CBG and the intra-class correlation at the CBG level which we conservatively defined as 0.1. The following formula was used to calculate the design effect: $DEFF = 1 + (n-1)\rho$ where $\rho$ is the intra-class correlation. Estimating 10 HHs per CBG, $DEFF = 1+ (10-1)*0.1 = 1.9$

Given these requirements, we anticipate approaching over 3,000 households (initially by mail). We expect a 50 to 60% non-response rate for a goal of enrolling approximately 1,386 households which includes 5,544 people (estimating 4 people per household). Given a potential 5% refusal for biologic sample collection, this leaves 1,317 households

**Phase II:**

Phase II participants are subject to an estimated 20% attrition over one year, thus we expect 1,053 households to have a 6-month follow-up visit with biologic sample collection.

With an effective sample size of 554 households, if the prevalence of testing is 10% in a reference group, we will be able to detect a difference given prevalence of 18.5% in a comparison group of participants, for a difference of 8.5% with 80% power and an alpha of 0.05. This same effective sample size translates to 80% power to find a difference between two groups with testing prevalence's of 5% and 11.5%, and testing prevalence's of 15% and 25%. For this effective sample size of 554 households, we expect a 50-60% non-response rate at baseline, which will require approaching 2,772 households for the successful recruitment and baseline participation of 1386 households. Given that we will recruit all household members, this may yield as many as 3,465 individuals enrolled at baseline (the average household population size is 2.5 in Baltimore City). Because we anticipate a very high intra-class correlation among household members, sample size is calculated at the household level.

For Phase II, we also calculated power for comparing the primary outcome related to randomization (proportion who complete SARS-CoV-2 testing) across arms (Arm 3 vs. Arm 1 and Arm 2 vs. Arm 1). Given that we enroll 1300 households in these three arms, and that we randomize arm at the household level, we will be able to detect a difference in the level of testing in Arms 2 or 3 and the control arm (Arm 1) of approximately 11%, (from 50% in the control arm to 61% in the comparison arm) with at least 80% power. We assume an overall type one error of 0.05, and control for multiple comparisons with the Bonferonni correction. Testing for individuals in the same household may be highly correlated, and so we conservatively assume that each household only enrolls one individual. This detectable

difference of 11% corresponds to a prevalence ratio of 1.2 given that testing prevalence is 50% in the control arm, to as low as 1.17, for a testing prevalence of 70% in the control arm.

**Statistical plan and data analysis:**

Descriptive analyses will be used to characterize the households sampled and the individual characteristics within households. Populations will also be characterized by neighborhood factors of interest.

**Phase I**

The primary analysis for objective one will calculate the prevalence of SARS-CoV-2 infection and associated correlates at a household level. We will use multi-level poisson and/or negative binomial regression to characterize individual and household factors associated with prevalence with random effects to account for clustering within the household and neighborhood. Regression models will also incorporate sampling weights to account for oversampling of certain populations. Individual characteristics of interest include demographics, occupation and employment status and knowledge and adoption of preventive measures. Household characteristics of interest include composition, infection status of household members and household adoption of preventive practices. Neighborhood factors of interest include neighborhood deprivation, poverty, and racial distribution.

Incidence analyses will consider new cases at an individual level and also at the household level. Incident cases will be defined as those who are RT-PCR and antibody negative at baseline and are positive for either antibodies or RT-PCR at any follow-up visit. We will characterize incidence per 100 person-years for the full sample and identify risk factors for infection using multi-level poisson and or negative binomial regression models accounting for clustering at the household and neighborhood level. Factors of interest to be included in the model include fixed characteristics such as demographics and time-varying characteristics such as occupation and employment status, chronic conditions, adoption of preventive measures. Similar to the prevalence analysis we will also include household factors including prevalent or incident infections among household members. Neighborhood factors of interest include neighborhood deprivation, poverty, and racial distribution.

**Phase II**

For objective 2, we hypothesize that compared to the SOC arm, those randomized to the mobile van testing arm will be more likely to receive their results within 5 days of randomization; however, those randomized to the home-based testing arm will be less likely to receive their results within 5 days despite greater acceptance of testing**.** Our analysis will compare the effect of each of the two testing modalities (mobile van testing, home-based testing) and the SOC (fixed site testing) in analyses summarizing the proportion receiving results within 5 days at the cluster level. We anticipate approximately equal sample sizes in each cluster, but if unequal we will include the number of participants in the regression. This regression will test the null hypothesis that the observed difference with the SOC arm is statistically different from 0 for each of the two testing modalities. Because we are *a priori* matching on factors anticipated to be correlated with the primary outcome (e.g., timely completion of testing with receipt of results), we will assume that factors salient to testing access will be balanced across arms and so proportions will be directly comparable without adjustment. However, there may be other confounding factors present (e.g., unforeseen local outbreak). To adjust for these differences, we will use a two-stage procedure.[48] After fitting the logistic regression model, we will compare the fitted and observed values by calculating a residual for each matched pair (as the difference between observed and expected). In the

second stage, these residuals are used to adjust the estimate of the pairwise differences. Importantly, we will not adjust for any post-randomization variables, only covariates measured at baseline.

Additional outcomes of interest will be calculated longitudinally including the prevalence of households and work-eligible individuals who experienced loss of employment due to COVID-19-related layoffs and similarly, loss of housing (such as an eviction) and the prevalence of reports of food scarcity.

**In-depth Interviews**

Data analysis will be guided by an iterative constant comparison approach informed by grounded theory. An iterative coding process in Atlas.ti will be used to conceptually name the data and reduce it to manageable units of information that cover broad and general categories. Codes will be informed by the questions in the qualitative guides as well as emerging ideas from the data, ensuring that the knowledge assembled from the observational data is not subjected to the themes solely established through the interview guide. Emergent themes can also lead to additional questions for subsequent interviews. Two coders will conduct open coding on three transcripts to the develop coding scheme. After discussion and development of a draft coding scheme, two more interviews will be coded and these will be further discussed to inform the initial coding schemes under Dr. Grieb's guidance. Through weekly virtual meetings, a team approach to data analysis will be employed, whereby different analysts provide feedback on emerging interpretations and check emerging categories against the raw data. In this way, an "audit trail" will be used to help ensure trustworthiness of findings, gather input from multiple perspectives, and enhance reliability. This process will continue until the information is saturated.

**d.** Early stopping rules. **N/A**

8. **Risks**

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Potential risks include:

Risk associated with **survey collection**: Participants will be informed that they may get tired, bored, or uncomfortable when they are completing questionnaires over the phone or online.

Risk associated with baseline, interim and 6-month **sample collection**: Participants may experience slight discomfort associated with blood being drawn, which are the same as standard clinical care. COVID-19 swabs, particularly placement in the nasopharyngeal site (NP swabs), may be uncomfortable for the participant.

Risk for **COVID-19 exposure** during clinical site visit to JHU: All household members coming to a JHU research site will be using the same space as our clinical services (i.e., outpatient screening tents). This offers a theoretical risk of exposure to COVID-19 through asymptomatic staff members. Screening will be completed prior to entering the van and appropriate PPE will be worn and cleaning protocols will be utilized (see below).

Risk for **breach of confidentiality**: Participants personal health information will be collected via standardized questionnaire and clinical specimens. We will also need to access their medical record for some forms of data collection.

b. Steps taken to minimize the risks.

**Survey collection** will occur via online, phone or paper mechanisms from the comfort and privacy of the participants. All staff will be trained on appropriate survey collection techniques to minimize participant burden. Staff will also provide resources to participants that can assist with issues that arise during any survey responses – mental health resources, housing, food, etc. Participants expressing concern over violence, suicidal thoughts, or major depression will be immediately referred for support to the principal investigator team, who will offer appropriate referrals to supportive counseling and/or violence resources, or as needed contact 911.

Staff training on **sample collection**: All staff will be trained by co-PI Farley who has led collection of COVID-19 specimens for JHMI with NP swabs, Middle Turbinate Swabs and Oropharyngeal Swabs. He will also train on all venipuncture procedures in addition to the completion of the JHH phlebotomy course if not already trained. Staff will follow a standard operating procedure and will have the appropriate credentials and/or training to collect each sample. Each staff will have completed blood borne pathogens training along with all infection control trainings related to personal protective equipment. A chain of custody document will guide all sample processing, labeling and delivery procedures.

**COVID-19 Exposure**: All participants will receive verbal instructions to follow before arriving to the JHMI testing site, mobile van and prior to being administered the home kit. These steps are outlined by study arms below:

Fixed Site Testing (Arm 1):

1. Transportation: We will encourage use of a personal vehicle, but this may not always be possible. Masks/hand hygiene during transit: Participants will be encouraged to use a mouth covering in public areas while coming to the research testing tent site.
2. Testing Tent Site Hand hygiene: There will be a research booth set up within the testing tent site. A research assistant will greet the household/individual on arrival to the testing tent and offer alcohol-based hand sanitizer to each person. Participants will also be instructed to use alcohol-based hand sanitizer prior to entering and after leaving the site.
3. Masks at testing site: a research assist will provide a paper-mask to each person to use and take home with them.
4. Specimen collection for COVID-19: Collection of all specimens for COVID will occur outside in the secure, private area of the testing tents, out of the public eye to protect privacy, while reducing viral contamination.
5. Research staff will use an N95 with eye protection following the same standard as community-based collection sites.

Mobile Van Testing Site (Arm 2):

1. Symptom screening: The first step of this process will be symptom screening of all household members. Households where any member reports symptoms will be immediately referred to the PUI testing area at the mobile van.

Hand hygiene: A research assistant will greet the household/individual outside the van at a registration table and offer alcohol-based hand sanitizer to each person.

3. Masks at mobile van site: A research assist will provide a paper-mask to each person prior to entering the mobile van.
4. Participants will not enter the van.
5. Respiratory or saliva specimen collection for COVID-19: Collection of all specimens for COVID will occur outside in the van in a designated area, out of the

public eye to protect privacy, while reducing viral contamination inside the research site.

6. Research staff will use the following PPE based on exposure risk:
   All van research members, regardless of role: N95 with eye protection following the same standard as community-based collection sites.

Home Testing (Arm 3):

1. A standardized educational handout will be provided to instruct the participant on all aspects of specimen collection.
2. Although the location of specimen collection is the participants home, this handout will include instructions to avoid collection within the home environment in order to limit environmental contamination and exposure to others in the home.
3. Instruction will also include details on hand-hygiene before and after collection and prior to handling mailing materials.

Strategies to prevent **breaches of confidentiality** in data: As with any study, standard procedures to protect privacy will be in place. We will use a participant ID number on all study related documents and samples. Only the study coordinator and PI team will have access to link participant ID number to participant names. All data will be entered into a secure REDCap data base that is password protected, encrypted and ran on secure JHU servers.

Strategies to prevent **breaches of confidentiality** in the community: Our mobile van will not identify COVID. We will only wear medical grade PPE inside the van. A staff member greeting the participants outside the van will use a standard paper-based mask – as consistent with the governor's recommendations.

c. Plan for reporting unanticipated problems or study deviations.

   Adverse Event Reporting: Due to the low-risk nature of the interview and standard of care collection methods for any specimen collection, we do not foresee adverse events occurring during this component of the research protocol. However, any adverse events (including participant expressions of discomfort during or after interview) will be documented and stored in study folders. Adverse events will be reported to the IRB in accordance with University Policies and Procedures.

d. Legal risks such as the risks that would be associated with breach of confidentiality.

   While we do not anticipate any issues of confidentiality issues. All participants will be given the option of a visit to the JHU research site or mobile van, to align with individual household comfort levels.

   Regarding the qualitative work (in-depth interviews) we will take several steps to reduce the risk of confidentiality breach. Staff will upload recorded audio files onto an encrypted network maintained by Johns Hopkins that meets security standards for PHI and is backed-up each night and will delete the files from the recording device. Digital records will be transcribed for data analysis. After each interview, the audio-recording will be transcribed by a company that has a signed confidentiality agreement with the Johns Hopkins University; a copy of this signed agreement is attached as a supplemental study document. The digital recordings will be deleted from the network and the conclusion of the qualitative data analysis

e. Financial risks to the participants.

We are aware that a positive COVID-19 PCR indicates active infection and may prevent the individual from returning to work. This is an important implication of this work along with public health practice for identifying and isolating cases. We are hopeful that antibody testing might also help to provide individuals with information to consider when thinking about returning to their work environment.

9. **Benefits**

a. Description of the probable benefits for the participant and for society.

This study has no direct benefit to the participant; however, a large societal benefit is anticipated. Increased knowledge of testing practices along with barriers, facilitators and predictors of testing is anticipated. We also seek to understand the impact of testing status (i.e., PCR or antibody positivity) on non-pharmaceutical intervention adherence behaviors.

10. **Payment and Remuneration**

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

Each person in the household who completes the baseline survey will receive $50.

Each person that completes the baseline testing visit will receive $50.

Every month, every household member will receive an additional $25 for completing 3 brief weekly questionnaires and $25 for a monthly questionnaire. Each household member will receive $25 for up to 6 interim testing visits, and after the 6$^{th}$ visit, no additional payment will be provided for interim visits prior to January 3, 2022. After January 3, 2022, we will no longer provide compensation for interim visits.

For the 6-month final visit each household member will receive an additional $100 for completing a survey and a testing visit.

Reimbursement for those under the age of 18 will be given to the parent/legal guardian. Payments will be in the form of gift cards.

Participants who complete an in-depth interview will receive $40.

Individual members of the household that receive over $599 in payment in a calendar year are required to report this income as taxable in the state of Maryland.

11. **Costs**

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

All laboratory testing will be covered by the study. There will be no direct cost to the participant.

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