

# Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) SARS-CoV-2 Household Transmission Study

Version 1.0

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## 1.3 Abt Associates

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## 2. Background

Clinical trials for licensure of COVID-19 vaccines will measure vaccine efficacy against laboratory-confirmed COVID-19 associated illness in the study population. Following vaccine licensure, large cohort studies are planned to estimate the effectiveness of COVID-19 vaccines for the prevention of SARS-CoV-2 infection by conducting routine swabbing of asymptomatic participants in addition to testing symptomatic participants. Vaccination may also have an effect on transmission of SARS-CoV-2. This effect has important implications if COVID-19 vaccines are less than 100% effective against either infection or illness, leading to some vaccinated individuals having breakthrough infections that can be passed to close contacts and family members.

The currently ongoing RECOVER (Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel) cohort study is designed to estimate the incidence of symptomatic and asymptomatic SARS-CoV-2 infection among essential workers. The study will also assess the COVID-19 vaccine effectiveness (VE) in preventing SARS-CoV-2 infection. This same platform can also be used to examine the frequency of infections that occur within households of participants after their index infection is diagnosed. If COVID-19 vaccine reduces the amount or duration of viral shedding among infected individuals, we would expect to identify fewer subsequent infections within a household among vaccinated compared to unvaccinated essential workers.

Essential workers include health care workers, first responders, public safety officers and workers in critical infrastructure and services eligible for COVID-19 vaccination as determined by public health authorities. Index cases with laboratory confirmed SARS-CoV-2 infection or illness will be identified among eligible essential workers who test positive for SARS-CoV-2 infection. Index cases residing with at least one other person of any age will be invited to participate; each eligible household member will then be invited to participate. A short period of follow-up will occur to identify new respiratory virus infections among household members. Evaluating SARS-CoV-2 transmission within households of vaccinated and unvaccinated RECOVER participants will further inform the effectiveness of COVID-19 vaccination against SARS-CoV-2 transmission.

## 3. Objectives

The purpose of this study is to assess the frequency and timing of SARS-CoV-2 infections within households of participants with PCR-confirmed infections identified through respiratory specimens collected through weekly surveillance or as part of illness assessments, and in doing so:

- 1) Estimate the secondary or subsequent rate of SARS-CoV-2 virus infection within a household following a lab-confirmed infection from an index participant;
- 2) Estimate the ratio of secondary household SARS-CoV-2 infections among vaccinated compared to unvaccinated participants;
- 3) Estimate the COVID-19 vaccine effectiveness (VE) in preventing secondary infections within households.

## 4. Definition of Common Terms

Several terms are used commonly throughout the study protocol, and below are their definitions.

*Household*: a shared living space between  $\geq 2$  people, excluding correctional facilities, long-term care facilities, boarding schools, hostels, dormitories, or other similar institutionalized settings

*COVID-19-like illness*: any person with SARS-CoV-2 infection by RT-PCR conducted on study-collected specimen (any) where onset of at least one of the following symptoms was reported within 7 days of sample collection: fever, chills, cough, shortness of breath, sore throat, diarrhea, muscle or body aches, and change in smell or taste

*Index participant*: the individual currently participating in RECOVER with laboratory-confirmed SARS-CoV-2 virus infection

*Household member*: any person who regularly spends at least half of their time in the household

*Secondary attack rate*: The secondary attack rate is the proportion of all enrolled household members who were not ill at the time of illness onset in the primary ill person who developed laboratory-confirmed SARS-CoV-2 virus infection after illness onset in the index participant

## 5. Study Design

The current study intends to collect daily respiratory specimens for 10-days from all household members after an index participant is diagnosed with PCR-confirmed SARS-CoV-2 infection. Thus, household participation is initiated when a RECOVER enrollee is diagnosed with PCR-confirmed SARS-CoV-2 infection from either routine weekly respiratory specimens or an illness specimen. Once an infection is identified, participants with at least one household member will be contacted by study staff to explain the purpose and activities of the study, determine interest in participation, and enroll both the RECOVER index case and household members into the study. Upon completion of consent to participate, a brief enrollment interview is given to ascertain demographics, vaccination status, and prior SARS-CoV-2 infection among household members. The presence of illness among any household member will be assessed for the two weeks prior to the start of the household assessment and illness symptoms will be assessed daily.

### 5.1 Study Population

RECOVER (Research on the Epidemiology of SARS-CoV-2 in Emergency Response Personnel) is a longitudinal cohort study representing a 3,450 healthcare, first responder, and other frontline workers across six geographic areas in the United States. The RECOVER study will identify asymptomatic and symptomatic infections, estimate laboratory-confirmed SARS-CoV-2 incidence, and characterize the humoral and cellular immune responses to both SARS-CoV-2 infection and vaccine. The information gathered will inform duration of protective antibody associated with infection and vaccination, vaccine effectiveness, and will further aid in future planning for pandemics. Participants are contacted on a weekly basis to assess symptoms and provide a nasal swab specimen. Blood specimens are collected

from participants quarterly, at convalescence upon infection, and following each vaccine dose. Receipt of COVID-19 vaccine will be documented using multiple methods, including linkage with immunization information systems, electronic medical records and employee health immunization records linkage, participant-provided documentation, and participant report.

### 5.1.1 Inclusion Criteria

All RECOVER participants with at least one household member reported during RECOVER enrollment are eligible to join in the household study, regardless of vaccination status. The household study will be triggered by a PCR-positive SARS-CoV-2 result in the RECOVER participant, unless they indicated they do not want to be contacted for further studies.

An **index RECOVER participant** is eligible to be included in the study if s/he:

- has at least one household member, regardless of whether or not other household members agree to participate in this study
- has not opted out of contact for future studies

A **household member** is eligible to be included in the study if s/he:

- regularly spends at least half of their time in the household

### 5.1.2 Exclusion Criteria

An eligible **index patient** will be excluded from the study if s/he:

- does not live in a household (e.g. lives in a correctional facility, skilled nursing facility, long-term care facility, boarding school, hostel, or in a dormitory)

## 6. Study Procedures

### 6.1 Study Period

Enrollment of households will begin as soon as IRB review and approval.

### 6.2 Identification of Index Participants

Index participants will be identified through RECOVER testing procedures, including PCR testing of routine weekly self-collected respiratory specimens or self-collected respiratory specimen that are participant-initiated upon illness. Results from the CDC-designated central laboratory are reported back to sites daily for rapid identification of SARS-CoV-2 infections as described in Section 6.7.2.

RECOVER participants who self-report a documented positive molecular test that was not conducted through the RECOVER study may be approached to begin information and consent process, pending confirmation of PCR-infection from a study-collected specimen.

## **6.3 Recruitment**

### **6.3.1 Circulation of Advance Materials**

Participants of RECOVER will be informed of the household transmission in advance and asked to make household members aware. Participants may be provided a fact sheet describing the household study and providing an outline of the study activities. Materials to share with the household may also be made available for the participant to share with their household if they choose to do so.

### **6.3.2 Index Participant**

Once a RECOVER participant has been identified with PCR-confirmed SARS-CoV-2 infection (“index participant”), study staff will contact the index participant to briefly describe the household study, answer any questions, and initiate consent procedures. If more than one RECOVER participant lives in the household, the participant testing positive first will be considered the index participant.

## **6.4 Enrollment**

### **6.4.1 Informed Consent – Index Participant**

Informed consent must be obtained from the index participant prior to contacting household members or may be obtained simultaneously. Household members will not be separately contacted about the study prior to obtaining consent from the index participant. Study staff will review study requirements with the index participant and each eligible household member and obtain and document consent and assent for children (Appendix A: Adult Informed Consent, Appendix A1: Parent Consent Form, Appendix A2: Verbal Assent Form). The consent form will document that all participants aged 18 and older have read and understood the consent and HIPAA authorization, that they have had all of their questions/concerns about the study answered, and that they have consented to participate in the study. Each adult participant in the household will provide informed consent for themselves and for any children <18 years of age for whom they are parent or legal guardian. Verbal assent of participants aged 7-17 years will be documented according to site requirements. To facilitate informed consent during a period of enforced social distancing and/or shelter-in-place orders, participants can provide verbal consent by telephone, video conference, or written/electronic signature consent by email or using an online electronic interface. All participants will be provided an electronic copy of the consent form.

Study staff will emphasize the voluntary nature of the study, the possible benefits and outcomes, alternatives to participation, confidentiality of participation, and the participant’s right to refuse and/or withdraw from the study at any time. It will be explained to participants that discontinuation of participation or choosing not to participate by index participant and/or household members will neither affect the employment status nor RECOVER participation status of the index participant. Upon complete review of these materials, documentation of participant consent will be written, electronic, or verbal. All participants will provide consent to be in the study. This consent will include authorization to provide the following:

- Permission to be contacted for study interviews among adults



- Daily self-collection of mid-turbinate nasal swabs for SARS-CoV-2 detection for a period of 10 days starting from the date of study supply receipt
- Archiving residual clinical and/or research specimens at the research site or CDC
- Permission for review of immunization and medical records (as available in EMR sites)

### **6.4.2 Household Information Form**

Once the index participant provides consent to participate in the household study, study staff will complete Appendix B: Household Information Form by phone interview. This form asks the index participant to confirm their household characteristics and composition, including the number of household members, their ages, gender, relationship to the index participant, and if their household members might be interested in participating in the household study. Contact information for adult household members interested in participation will be collected to obtain informed consent.

### **6.4.3 Informed Consent – Household Members**

Once the index participant has consented to the household study, consent procedures will be initiated for the index participant’s household members. Other members of the index participant’s household may be recruited into the study during the time of initial contact or an agreed upon alternate time within two business days.

Study staff will attempt to approach and recruit all members of an eligible household that the index participant has shared the contact information for with the household member’s permission; households with non-enrolling members will not be excluded. Household members who are not present during the initial contact for household enrollment may be consented and enrolled up to day 5 of the follow-up period, defined as the first day of specimen collection for the household.

If no household members consent to participate in the study, the index participant will still be enrolled and can continue the household study activities.

### **6.4.4 Participant Orientation**

Once informed consent has been obtained, participants will receive instructions about how to self-collect, store, package, and ship daily respiratory specimens according to study standard operating procedures. Participants will be given enough supplies for the period of follow up for each consented household member’s specimen collection. Household members consented later will receive enough supplies for the remainder of the follow up period for which they are participating.

Participants will be provided detailed written and visual instructions for collecting, storing and submitting respiratory specimens according to site-determined methods, including facility drop-off, courier pick-up, or shipping the specimens according to local requirements. For virtual enrollment and follow-up, this may include a video interaction such as FaceTime, Zoom, and/or other video conferencing mechanism. Videos that participants can watch during their own time may also be used.

### **6.4.5 Household Reporter**

During the consent and enrollment process, a member of the household can be identified as the household's primary point of contact ("household reporter") for study-related communications. The household reporter can complete Appendix D: Household Study Enrollment Interview on behalf of other household members. As the index participant may be ill, this may be another adult (age  $\geq 18$  years) household member. The household reporter will be responsible for ensuring adherence to daily study procedures for the household unit.

## **6.5 Data Collection**

Prior to the household study, RECOVER participants (the index participant) or their designated household reporter will provide demographic and household characteristic data and details about their current illness through collection instruments defined in the RECOVER protocol (Acute Illness, Illness Update, Illness Recover, and/or PCR Positive Survey if asymptomatic).

Data will be collected for this household study through Appendix B: Household Information Form (Section 6.4.2), Appendix D: Household Study Enrollment Interview, Appendix E: Specimen Data Sticker, and Appendix F: Follow-Up Interview. All surveys and interviews will be administered by telephone; however, online instruments may be used if a participant is unable to complete an interview. Additional data collection of demographic characteristics, medical history, medical utilization, clinical SARS-CoV-2 and influenza lab testing results and vaccination history may be accessed from medical records with the participant's consent. All responses will be stored in a secure web platform.

### **6.5.1 Enrollment Interview**

Following the provision of informed consent of other adult household members, participants will be briefly interviewed by phone (Appendix D: Household Study Enrollment Interview), or may allow the household reporter to provide responses, as indicated in the consent form. Parents/guardians of children aged  $< 18$  years may complete their interview questions, as preferred. The Household Study Enrollment Interview will be completed for all household members other than the index participant.

The interview questions will ask if any household member has tested positive for SARS-CoV-2 previously or had any illness in the two weeks prior to the index participant's illness onset (or positive specimen collection). Additional questions will collect COVID-19 vaccination status and doses received; race/ethnicity of each household member will be collected at the discretion of each study site.

### **6.5.2 Specimen Form**

A specimen collection form will be collected with each participant's daily specimen (Appendix E: Specimen Data Sticker). Participants are asked to indicate the day their specimen was collected and the presence or absence of symptoms (fever, chills, cough, shortness of breath, sore throat, diarrhea, muscle or body aches, change in smell or taste, or felt ill in any other way).

### **6.5.3 Follow-up Interview**

At the end of the follow-up period, the case definition reports from the specimen forms will be examined for each of the 10 days for household members with SARS-CoV-2 detected on any daily

specimen during the follow up period (Appendix F: Follow-Up Interview). If case definition information is missing for any of these 10 days (e.g., due to failure to complete question on specimen form or failure to submit swab) and the participant's SARS-CoV-2 PCR test is positive, the household reporter or household member will be asked to clarify their health status on the missing day.

#### **6.5.4 Medical Records**

Among sites/participants with EMR data available, permission will be requested from participants to access medical records. With permission, data will be extracted to supplement self-reported information on health status, COVID-19, influenza, and pneumococcal vaccination status and history, and medical care utilization.

Data from the EMR will be extracted to count medical visits for acute illness and chronic medical conditions for the 12 months prior to enrollment and through the end of the study year using (a) International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes for all ambulatory medical encounters, (b) ICD discharge codes for all hospital admissions.

Additionally, for participants with rRT-PCR-confirmed SARS-CoV-2 or influenza infection, all EMR sites will provide information from medical encounters between the date of onset through illness resolution or two weeks from the date of PCR detection for asymptomatic participants (Appendix G: Electronic Medical Record Extraction Data), including dates of visits, ICD code diagnoses, clinical diagnostic testing for respiratory pathogens (and results of testing if feasible), CPT codes for chest and sinus radiography, ICU admission, and ventilator support. Further information on therapeutic interventions will be extracted, including but not limited to antivirals, antibiotics, steroids, and other COVID-related therapeutics.

#### **6.5.5 Vaccination**

COVID-19 vaccination status of household members will be documented by self-report or via the household reporter. Vaccinated household members will be asked to report on the name, dose, and date of their vaccination from their vaccination cards. If possible, households will be asked to share digital images or other direct documentation of these cards. All consenting household members will also be asked for permission to confirm COVID-19 vaccination status using the electronic medical or employee health record or state registry data.

### **6.6 Specimen Collection**

Enrolled household study participants will self-collect a standard respiratory specimen, and ship to a CDC-designated laboratory that is clinical laboratory improvement amendments (CLIA) certified for SARS-CoV-2 testing. During this study, a standard respiratory specimen is defined as a participant or guardian-collected mid-turbinate nasal swab using a flocked nasal swab or equivalent based on available data about SARS-CoV-2 detection. If emerging data indicate that other specimen types, such as saliva or foam swabs, are comparable or superior to current specimen type or procurement of flocked nasal swab supplies is not possible, the study will modify the choice of standard respiratory specimen accordingly.

Any modifications to sample collection will be determined and approved jointly by site teams, Abt, and CDC.

Participants will be asked to self-collect a respiratory specimen each day for 10 days, regardless of infection status and beginning on day of supply receipt. At the start of surveillance, participants will be given enough supplies for each household member to collect daily specimens for 10 days and written and/or visual instructions for collection and shipping. The supplies will include the appropriate collection items for the nasal swab with room temperature transport medium, interior specimen packing materials, and packaging materials for shipping the specimen. During summer months, we expect all shipments will have to include a cold pack to avoid extremely high temperatures during shipment.

Sites may establish a courier service to collect specimens from participants homes each day, designate drop-off locations for kits within their facilities, or participants may ship via express mail to the central reference laboratory.

Figure 1 illustrates an approximated timeline from index participant onset for household enrollment, kit allocation and specimen collection. Days 1 through 4 represent the time between a RECOVER participant experiencing illness, collecting a swab for testing at the CDC-designated laboratory. In this example, Day 5 represents the day PCR results are reported and study staff reaching out to the index RECOVER participant. If household enrollment and kit delivery can be completed in a single day, Day 5 would be the household’s 10-day start date. Additional rows demonstrate the number of days from illness onset given variation in all dependent time factors.

**Figure 1. Timelines describing follow-up periods**

Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	
Index Onset	Swab collection, shipping			PCR Result	Follow-up period from day specimen collection kit is received to a 10th collection day													
				Kit receipt Swab 1	Swab 2	Swab 3	Swab 4	Swab 5	Swab 6	Swab 7	Swab 8	Swab 9	Swab 10 End					
					Kit receipt									End				
						Kit receipt									End			
							Kit receipt									End		

## 6.7 Laboratory Assessments

### 6.7.1 Molecular Assays

The CDC-approved, CLIA-approved reference laboratory will perform a CDC-specified rRT-PCR assay to

ascertain infection with SARS-CoV-2 and other respiratory viruses such as influenza, RSV etc. Testing will be completed using CDC protocols and with primers, probes, and reagents provided by the CDC. Additional testing for other common respiratory pathogens including influenza, parainfluenza viruses, human metapneumovirus, adenoviruses and other coronaviruses may also be conducted. Additional virus characterization including measurement of viral quantity by quantitative-PCR and/or sub-genomic virus RNA (sgRNA) through specialized PCR assays may also be conducted. Remaining aliquots of all study specimens will be sent to a CDC-designated facility for additional virus characterization (including but not limited to viral isolation, and novel severity markers), banking and storage; no specimens will contain personal identifiers.

### **6.7.2 Reporting of SARS-CoV-2 rRT-PCR Results**

The reference laboratory will provide daily updates to the central data management system and study staff of rRT-PCR results. The lab processing participant samples is a CLIA approved CDC-reviewed lab that is applying EUA methods and standard best practices for lab QA/QC to minimize the possibility of reporting false positive results. QA/QC checks are built-in to the process and will not impact the timing of the lab's reporting results to the study sites. All participants will be informed of the results in accordance with site-specific policies. In most instances results will be available in less than 48 hours from sample collection. However, some results may take as long as a week depending on time shipping time, lab volume, etc.

All adult household members will receive their SARS-CoV-2 PCR results according to site-specific methods as detailed in the Local Context Form, including directly via email, patient message in the local electronic medical record application, and may also be called for notification of a PCR-positive test result. All results for minors in the study will be reported to a designated parent or guardian. All positive SARS-CoV-2 PCR results will be reported to the local/regional health department. Depending on site, study staff will not inform the employer or daycare/school of any participant regarding their research test results. Molecular diagnostic results will not always be available during the period when participants are acutely ill. Participants will be informed that:

- Results are from a research laboratory and not meant to replace recommended clinical and/or occupational tests;
- False positive and false negative results are possible;
- If we are made aware of a false positive after notifying a participant of their results, we will notify them immediately, as well as any persons/institutions/agencies with whom the positive results were shared;
- Receiving a negative diagnostic result should not alter their preventive behaviors, given that results are specific to the date and time they are collected, and current assays may not be sensitive to all infections;
- Participants should consult their personal primary care provider if they have questions, concerns, or any medical needs related to their illness;
- If working in contact with other people, they should follow their employer's or daycare's or

school’s guidelines for reporting illnesses and returning to work/daycare/school.

There are potential benefits from reporting results to participants and minimal risks. Confirmation of SARS-CoV-2 infection may aid them in making decisions to prevent secondary exposure to family members, co-workers, patients, and/or members of the public.

## 7. Statistical Considerations

### 7.1 Sample size

#### 7.1.1 Outcomes and surveillance groups

This study has two primary outcomes of interest. First to determine the secondary attack rate of SARS-CoV-2 virus infection within a household following a diagnosed infection from an index participant. For this study, a new SARS-CoV-2 detection in a household member is defined by the individual having no detection in any swabs prior to a subsequent swab that tests positive by RT-PCR. Second, a proportional hazards model will be used to estimate VE in preventing secondary or subsequent household infections.

#### 7.1.2 Power Calculations

The combination of the RECOVER and the Arizona Healthcare, Emergency Response and Other Essential Workers Surveillance (AZ HEROES) cohorts provides the sample size needs for household enrollment of participants with SARS-CoV-2 detection. Vaccine will not be readily available at the start of the study but will be distributed to the cohort gradually. Subjects may change their vaccination status (i.e., vaccinated during follow-up) from unvaccinated to vaccinated, and contribute both unvaccinated and vaccinated person-time at risk. Thus, vaccination status is time-varying. Calculating statistical power with closed-form expression when exposure is time-varying is challenging. Instead, Monte Carlo simulation will be used to estimate the statistical power to detect the VE against any infection, symptomatic or asymptomatic. The simulation assumed a total cohort size of 5,000 participants and both 6-month and 12-month post-vaccination follow up periods. For the simulations, we assumed a monthly attack rate of 1% to 1.9% (or cumulative attack rate ranging from 8% to 17%). We allowed for 25% study attrition, and vaccination uptake according to the following occupational groups over the 12-month time frame.

		Quarterly Cumulative Vaccine Assumptions			
	% of total sample	Q1	Q2	Q3	Q4
<b>HCP</b>	<b>65%</b>	<b>50% ≥ 1dose 30% 2dose</b>	<b>75% ≥ 1dose 55% 2dose</b>	<b>85% ≥ 1dose 70% 2dose</b>	<b>90% ≥ 1dose 80% 2dose</b>
<b>FR</b>	<b>15%</b>	<b>35% ≥ 1dose 15% 2dose</b>	<b>50% ≥ 1dose 35% 2dose</b>	<b>70% ≥ 1dose 55% 2dose</b>	<b>85% ≥ 1dose 70% 2dose</b>
<b>EW/</b>	<b>20%</b>	<b>15% ≥ 1dose</b>	<b>30% ≥ 1dose</b>	<b>50% ≥ 1dose</b>	<b>70% ≥ 1dose</b>

FW		5% 2dose	15% 2dose	25% 2dose	40% 2dose
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The result for all simulations was  $\geq 99\%$  power to detect VE against any infection and an estimated approximately 80 vaccine failures and 230 infections among unvaccinated participants would occur. Extending the simulated case ascertainment to the VE against household transmission, with an average household size of 2 people per household, we estimated the power to detect VE against transmission (or subsequent household member positivity following index participant’s positive result)  $>80\%$  across simulations.

### 7.1.3 Vaccine and VE Objectives

VE against household transmission is defined as the reduction in likelihood of transmitting to someone in household given full vaccination.

$$HR = \frac{\text{Vaccinated} \frac{\# RECOVER \text{ infected and transmitted to HH}}{\# RECOVER \text{ infected and did not transmit} + \# \text{ uninfected}}}{\text{Unvaccinated} \frac{\# RECOVER \text{ infected and transmitted to HH}}{\# RECOVER \text{ infected and did not transmit} + \# \text{ uninfected}}}$$

Vaccine effectiveness will be calculated as:

$$1 - aHR * 100$$

The effect of the following covariates on VE estimates will be considered for all outcomes: site, age, household characteristics, and account for clustering by household. VE will be calculated by age group, full vs. partial vaccination, and vaccine type if multiple products are in use.

If any statistical method is found to be unsuitable during analysis due to unexpected recruitment or seasonal effects (e.g., inadequate sample size, low participation in surveillance), alternate methods will be used. Any changes in methodology will be documented.

## 8. Data Entry and Management

Each participating study site will maintain study databases on site. Tracking databases with participant identifying information and contact information will be kept securely according to the standard operating procedures of the local site with respect to cybersecurity, privacy, participant confidentiality, and compliance with applicable HIPAA regulations.

All survey data will be entered directly into the study REDCap database through online interviews/surveys, the secure text messaging interface, and/or the mobile application. Study site staff will enter response data directly into the REDCap database if interviews are administered by telephone or in person. The questions in the approved forms will appear on the REDCap data website rather than in paper form.

All study related documents and samples will contain a unique identifier per person. The online, mobile application, text message, and REDCap data entry screens will provide some quality assurance thorough

the use of logic and range checks and automated skip patterns. Additional quality checks of the data will be performed on a weekly basis including checks for out-of-range values and missing data.

Laboratory results from rRT-PCR assays will be entered directly into a REDCap laboratory database from the study reference laboratory or through the study coordinating center. Data from the laboratory REDCap database will be merged into the study database using the Specimen ID.

## 9. Human Subjects Issues

### 9.1 IRB Review

Prior to study implementation, the protocol, informed consent form, participant education and recruitment materials, data collection instruments and other documents associated with the protocol shall be approved by the institutional review board (IRB) overseeing each site’s study activities. Subsequently, all protocols must be re-reviewed at least annually. All protocol amendments must be approved by the IRB prior to implementation. The study sites and coordinating center are responsible for preparation and submission of all documents and periodic reports as required by their respective local IRBs.

US CDC determined (May 20, 2015) that the information collection activities conducted under this project qualify for the NCVIA-conferred Paperwork Reduction Act (PRA) waiver as they come under the activities authorized under the NCVIA at section 2102 (a)(7) of the Public Health Service Act (42 U.S.C. 300aa-2(a)(7)).

The table below indicates the IRB of record for the institutions participating in the RECOVER study.

<b>IRB of Record</b>	<b>Relying Sites</b>
Baylor Scott and White Health	Baylor Scott and White Health
Kaiser Permanente Northwest	KPNW, Abt Associates, CDC
St. Luke’s Hospital IRB	St. Luke’s Hospital
University of Miami	University of Arizona, University of Miami
University of Utah	University of Utah

### 9.2 Confidentiality

Each household member will be given a unique study ID which will be used on all study materials and specimens. The index participant will use their study ID from the RECOVER/HERORES study. Multiple forms of contact information, including telephone, email, mailing address and information from close/emergency contacts (e.g., spouse or other family members) likely to know how to reach the



participant should the study lose contact will be collected, but will only be accessible by local study staff. Only descriptive information included in the contact lists (non-identifiable demographic information and occupation) will be recorded for potential participants who cannot be contacted, are ineligible, or are eligible but refused participation, in order to examine potential participation or selection biases. Stated reasons for refusal will also be recorded.

All study data, laboratory specimens, reports, study data collection, study procedure, and administrative forms will be identified by a coded number only to maintain participant confidentiality. All study data will be stored separately from study records that contain names or other personal identifiers (such as locator forms and informed consent forms). All local databases must be secured with password protected access systems.

Forms, lists, logbooks, appointment books, and any other listings that link Study IDs to other identifying information must be stored in a separate, locked file in an area with access limited to local study staff. If participant names and corresponding Study IDs are entered into a computer database, this database must be password protected and must be maintained in a directory separate from any study specific data.

### **9.3 Benefits**

Participants will not personally benefit from participating in this study, other than potential remuneration selected by each site. There are potential benefits for reporting COVID-19 test results to participants. When results of SARS-CoV-2 testing are available, knowing the result may aid in making decisions to prevent secondary exposure to family members and other members of the public. However, the timeliness of notification of COVID-19 test results to participants will depend on reference lab capacity.

### **9.4 Remuneration**

Sites may determine the remuneration of study participants as small gifts or incentives to compensate for the time and effort involved in this study. Payments to reimburse participants for the costs of text messaging, cellular data usage, and phone calls is recommended. Further payments for compliance and milestones are recommended based on what is customary for that site, such as per respiratory sample per day during the surveillance period, and at the completion of milestone surveys. Sites may choose not to provide reimbursements for participation.

### **9.5 Risks**

Study investigators and institutions are committed to protecting personal health information through the maintenance of privacy and security of each subject's personal information in this study. To protect confidentiality, we will use a study assigned number instead of personal information on study forms and we will store data in locked files and/or secured computers. Any data collected that could identify individual participants will be destroyed when the study is done. If information from this study is presented publicly or published in a medical journal, individuals will not be identified by name or by any other personally identifiable information. The researchers in this study will be looking at personal health

information but will not disclose personally identifying information about individual participants to others.

Participants may experience mild discomfort or rarely a minor nosebleed associated with the self-administered daily nasal swab sample collection. In case of a nosebleed, the participant will need to apply steady pressure by pinching the nostrils together for 5 minutes to form a blood clot and spitting out any blood that may trickle down the throat.

Participants are at some risk regarding the confidentiality of their medical records. However, as noted above, no personal medical record information will be stored with any participant identifying information. Study staff responsible for collecting medical record information are all employees or contract workers of the local organization, which is providing health care to the participants.

Participants may be required to notify their employer if they test positive for SARS-CoV-2 and may be required to stay home from work as a result. Study sites will follow local policies for employer notification as outlined in the local context form.

## **9.6 Communicable Disease Reporting Requirements**

State or local health department regulations may require reporting of results from SARS-CoV-2 testing. Local investigators at each study site will be responsible for contacting their local public health departments to ensure study procedures comply with all reporting requirements.

## **9.7 Protocol Completion or Termination**

Study staff will complete a protocol completion or termination form for each participant at the time the participant either completes all protocol procedures or at the time of termination if early termination occurs. Sites will report deviations to their local IRBs according to site-specific reporting requirements and consult with Abt and CDC to adjudicate.

## **10. Data Sharing and Use**

Data and associated documentation from this study will be available only under a data use agreement developed by the steering committee and that provides for (1) a commitment to using the data only for research purposes and not to identify any individual participant; (2) a commitment to securing the data using appropriate information technology; and (3) commitments for destruction, return, or retention of data as stipulated by the steering committee.

Sites will comply with federal, state, and institutional requirements regarding time horizons for retention and/or destruction of research records.

## **11. References**

1. Centers for Disease Control and Prevention. Available at: [https://www.cdc.gov/vaccines/imz-managers/downloads/COVID-19-Vaccination-Program-Interim\\_Playbook.pdf](https://www.cdc.gov/vaccines/imz-managers/downloads/COVID-19-Vaccination-Program-Interim_Playbook.pdf). Accessed November 13, 2020.

## **12. Appendices**

Appendix A: Adult Informed Consent

Appendix A1: Parent Consent Form

Appendix A2: Verbal Assent Form

Appendix B: Household Information Form

Appendix C: Participant Information Form

Appendix D: Household Study Enrollment Interview

Appendix E: Specimen Data Sticker

Appendix E1: Specimen Color Key

Appendix F: Follow-Up Interview

Appendix G: Electronic Medical Record (EMR) Extraction Data