

Investigation of SARS-CoV-2 Seroprevalence and Factors Associated with Seropositivity in a Community Setting

Protocol Summary

Current epidemiologic data in the United States suggests that sustained community transmission of SARS-CoV-2 is occurring in certain areas. The extent of transmission of SARS-CoV-2 in community settings is currently unknown. Understanding the extent of transmission in communities is critical to inform decisions about prevention and control strategies as well as community mitigation interventions in the U.S. response to COVID-19.

The objectives of this investigation are to: (1) determine the extent of infection in communities as determined by overall SARS-CoV-2 seroprevalence; and (2) determine factors associated with SARS-CoV-2 seropositivity among persons residing in areas with evidence of community transmission.

A cross-sectional household survey design will be used to measure SARS-CoV-2 seroprevalence at one or more time points in ≥ 1 U.S. areas with evidence of community transmission of SARS-CoV-2. Areas with existing population-based surveillance platforms with well-defined catchment areas will be preferentially selected.

The investigation population will consist of all persons residing in selected households from selected defined geographic areas, according to the sampling framework.

The investigation will employ a multistage cluster sampling design using a modified CDC Community Assessment for Public Health Emergency Response (CASPER) framework. Thirty census blocks will be randomly selected from within the catchment area of each site. Seven households will be randomly selected within each census block. At least 210 households will be included in the sample from each catchment area.

Participants will be surveyed using a standardized questionnaire which will capture information on household characteristics, age, sex, race, ethnicity, exposures, underlying medical conditions and symptoms consistent with COVID-19 infection that occurred prior to the survey. Blood samples will be collected from all participants and tested for antibodies to SARS-CoV2 using an enzyme-linked immunosorbent assay with confirmatory microneutralization testing as needed.

The investigation will be managed by CDC, who will supervise CDC field teams.

The information obtained in this seroepidemiological investigation is needed to inform decisions about prevention and control strategies as well as community mitigation interventions. Further, the data obtained can inform burden estimates and modeling.

Abbreviations

CDC	Centers for Disease Control and Prevention
CLIA	Clinical Laboratory Improvement Amendments
DVD	Division of Viral Disease
ELISA	enzyme-linked immunosorbent assay
HCP	Health care practitioner
MNT	microneutralization testing
NCIRD	National Center for Immunization and Respiratory Diseases
PPS	probability proportional to size
WHO	World Health Organization

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Introduction

Current epidemiologic data in the United States suggests that sustained community transmission of SARS-CoV-2 is occurring in certain areas. The extent of transmission of SARS-CoV-2 in community settings is currently unknown. In the case of a novel virus, such as SARS-CoV-2, initial seroprevalence in the population is expected to be negligible; therefore, seroprevalence estimates can be useful to understand cumulative incidence in a given population.¹ Antibody seropositivity may also provide data about asymptomatic or subclinical infections that would not be detected by surveillance that relies on medical visits. These data could supplement medically attended infection rates and contribute to understanding the overall burden of COVID-19. This information could also contribute to modeling estimates to inform decisions about prevention and control strategies as well as community mitigation interventions in the U.S. response to COVID-19.

Objectives

- To determine the extent of infection in communities as determined by overall SARS-CoV-2 seroprevalence
- To determine factors associated with SARS-CoV-2 seropositivity among persons residing in areas with evidence of community transmission.

Methods

Survey design

A cross-sectional household-based survey design will be used to measure SARS-CoV-2 seroprevalence at one or more points in time.

Investigation location

The investigation will be implemented in ≥ 1 U.S. locations with evidence of community transmission of SARS-CoV-2. Locations with pre-existing surveillance platforms in place to capture COVID-19 hospitalization rates and well-defined geographically bound catchment areas will be preferentially selected for implementation.

Investigation population

The investigation population will consist of all persons residing in selected households from selected defined geographic areas. Individuals of all ages residing within an eligible household will be assessed for eligibility. An eligible household participant will be defined as an individual who spends an average of ≥ 2 nights per week in the home. Households will be defined as a shared living space between ≥ 2 people, excluding correctional facilities, long-term care facilities, boarding schools, hostels, dormitories, or other similar institutionalized settings. Households in which English is not the primary language spoken may be excluded from the survey if translation services are not available.

Sampling

Sampling methodology

The investigation sampling methodology will be based on a modified CDC Community Assessment for Public Health Emergency Response (CASPER) framework (<https://www.cdc.gov/nceh/casper/default.htm>).²

The investigation will employ a multistage cluster sampling design to obtain a representative sample of households. Counties within a selected catchment area will be identified. Using the most updated census data, census blocks will be selected according to probability proportional to size (PPS) within each county. Maps will be obtained for each of these census blocks and based on visual inspection, households will be manually labeled and numbered within each of these census blocks. A list of all the households will be created for each census

block (i.e. cluster) and seven households will be randomly selected using a random number generator. Selected households will be approached on at least three separate occasions before replacement due to non-availability.

Sample size

At least 210 households will be included in each catchment area sample. All eligible participants within a household will be approached for recruitment.

From a simulation of 450 people where seroprevalence is highly correlated within households ($r=0.8$), the expected margin of error is less than 10%. For example, if the seroprevalence was 20.0%, then the expected 95% confidence interval is (13.4%, 26.1%).

Table. Expected precision of seroprevalence with a sample size of 450 persons

Seroprevalence	Expected 95% Confidence Interval
0.1%	(-0.2, 0.4)
10%	(5.1, 14.6)
20%	(13.4, 26.1)
30%	(22.9, 37.6)
40%	(32.7, 48.4)

Data collection

Two standardized questionnaires will be administered: a household level questionnaire and an individual level questionnaire. One respondent in each household (an adult who knows about all of the residents of the household) will provide responses for the household level questionnaire and each household member (or parent guardian in the case of a child too young to answer) will provide responses for the individual level questionnaire (Appendix A). The household level questionnaire will capture information on household characteristics and document all household members whether they are present at the time of the visit or not. The individual-level questionnaire will capture information on age, sex, race, ethnicity, exposures, underlying medical conditions and symptoms consistent with COVID-19 since January 2020 for each available and consenting household member. The questionnaire will be administered by trained staff either in person. Team phlebotomists will collect up to 10mL venous blood (or for children the recommended volume per age and weight) from each consented participant in an enrolled household (see specimen collection section below).

Data collection teams will consist of two members: an interviewer and a phlebotomist. The interviewer will consent individuals and conduct the interviews and the phlebotomist will obtain blood samples. The phlebotomists will be professional nurses who will be contracted by CDC to participate in the survey.

Questionnaire responses may be collected using REDCap³, including possibly mobile data collection software. Paper forms will be used to collect consent and may be used to track visited households within a selected census block.

Data management

All data generated from this project will be managed and stored according to established data management principles. All hardcopy data will be stored in locked file folders in the field and later stored in locked cabinets at CDC.

Specimen collection, storage, handling, transportation and testing

- Blood will be collected from each participant using standard venipuncture techniques and following recommended PPE guidelines. Blood volume collected will not exceed the recommended amount per age and weight.
- Once collected, blood samples will be stored in closed cooler boxes in team vehicles and then transported to the local collaborating laboratory for processing.
- Testing will be done at CDC using serologic assays that test for SARS-CoV-2 antibodies. Serologic assays will likely include enzyme-linked immunosorbent assays (ELISA), and when necessary, microneutralization testing (MNT). As serologic tests are further developed, it is possible that additional serologic tests and quantitative testing for different classes of serum antibody might be performed.
- Currently, the available serologic assays have not been approved as diagnostic assays under CLIA regulations and individual results are not able to be reported back to participants. If CDC obtains CLIA approval for the SARS-CoV-2 ELISA, then CDC will be able to report back individual results. The option to have results returned to participants if the test is CLIA approved will be offered to participants.
- All personnel involved in the investigation will be trained in infection prevention and control procedures. Recommended personal protective equipment (PPE), which may include a surgical mask or N95 respirators, gown, gloves and a faceshield, will be used by staff and phlebotomists entering households. Procedures should include proper hand hygiene, the correct use of masks or respirators, and proper donning and doffing of PPE.

Data analysis plan

Categorical variables will be presented by frequency distribution (e.g., frequency counts, percentages, and 95% confidence intervals). Continuous variables will be presented by summary statistics (i.e., mean and 95% confidence intervals). Individuals will be classed as positive or negative for SARS-CoV-2 antibodies based on pre-determined cutoff thresholds of the available assays. Analyses to estimate seroprevalence of antibodies to SARS-CoV-2 in the survey areas will account for the 2-stage cluster design, applying weights as calculated during the sampling process (the inverse of the probability of selection for a given household within each census block). Wilson 95% confidence intervals will be presented. Associations between seroprevalence and other variables will be measured using logistic regression.

Data sharing and use

The results of this investigation will be shared within the CDC COVID-19 response and to participating state and local jurisdictions. Results of this investigation will also be communicated at scientific meetings and in publications. Findings of this investigation may will be used to update and improve the survey tools and design.

Investigation management

The investigation will be managed and supervised by the CDC COVID-19 response Epidemiology Task Force.

Ethical Considerations

Participants 18 years of age and older will be enrolled after written consent is obtained. Participants under 18 years of age will be enrolled pending consent from an adult member of the household and/or assent by the minor (Appendix B). Participants will be assigned a unique investigation number to maintain anonymity. Personal identifiers will be removed from the data upon completion of the investigation. As part of the survey instructions and consent process, participants will be informed that their participation is voluntary, and a lack of participation will not affect their or their family's health or education.

Serum specimens sent to CDC laboratory will be labeled with identification numbers, personal identifiers will not be sent to CDC laboratory. Participant households may receive information sheets about the investigation as well as about COVID-19 (e.g., how to prevent it and what to do if they are sick) (Appendix C).

Public health importance

The information obtained in this seroepidemiological investigation will be useful to inform decisions about prevention and control strategies as well as community mitigation interventions. Further, the data obtained can inform burden estimates and modeling.

References

1. World Health Organization. Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection. <https://www.who.int/publications-detail/population-based-age-stratified-seroepidemiological-investigation-protocol-for-covid-19-virus-infection> Accessed 3/7/2020.
2. U.S. Centers for Disease Control and Prevention. Community Assessment for Public Health Emergency Response (CASPER). (<https://www.cdc.gov/nceh/casper/default.htm>). Accessed 3/19/2020.
3. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* **2009**; 42(2): 377-81.

APPENDICES

Appendix A: Questionnaire

Appendix B: Consent and Assent Forms

Appendix C: COVID-19 Fact Sheet

DRAFT

Appendix A

DRAFT

Appendix B

COVID-19 Community Seroepidemiological Investigation Adults ≥ 18 years

Individual ID# _____

The Centers for Disease Control and Prevention (CDC) is working together with (state/local jurisdiction) to learn more about the spread of COVID-19 (also called SARS-CoV-2) in communities.

To do this, we are talking to randomly selection households about COVID-19. We want to get a better idea of how many people in the community have been infected with SARS-CoV-2 (the virus that causes COVID-19), which will help the CDC and other public health officials make decisions about next steps in the response to COVID-19. Your house is one that has been randomly selected in your community. Participation is entirely voluntary. If you agree to participate, we will conduct an interview with you using a standardized questionnaire that includes questions about the people in your household and about yourself, including about your health. You can choose not to answer any questions that you might be uncomfortable with. We will also collect a tube of blood to test for antibodies that would indicate past infection with SARS-CoV-2. This will not tell us if you are currently infected with SARS-CoV-2. Risks of blood collection include discomfort with the needle stick, a small risk of bruising, redness or swelling around the site, a small risk of feeling lightheaded or fainting when the blood is drawn, and a rare risk of infection. There is no direct benefit to you from the blood draw, but your participation will help us learn more about COVID-19 and its spread in communities.

If you agree to participate, we will send your blood sample to the Centers for Disease Control and Prevention in Atlanta, GA for testing for antibodies to SARS-CoV-2. We will store what is left of the blood sample for other studies that we may do in the future related to the virus SARS-CoV-2. All your records, samples, test results, and interview answers collected for this investigation will be kept private.

The testing method for antibodies to SARS-CoV-2 is still being developed and is not yet an approved diagnostic test (CLIA approved test) as of 4/20/2020. CDC is working to obtain CLIA approval. CDC might get approval and if CLIA approval is obtained, individual serology results could be reported back to participants. The timeline for potentially being able to report results back is expected to be up to several months.

The results of these tests will help us understand how many people in a community have already been infected with SARS-CoV-2, which is important information to help public health officials make decisions about next steps in the response to COVID-19.

Your participation in this investigation is voluntary, and you may change your mind and decide not to participate in this part of this investigation. The interview and blood draw are expected to take about 30 minutes per person. If you have any further questions, you may call (state/local jurisdiction/CDC) at xxx-xxx-xxxx.

1. Have all of your questions about this public health investigation been answered?
 Yes No
2. Do you agree to be interviewed?
 Yes No
3. Do you agree to have a blood sample taken?
 Yes No
4. Would you like to obtain your individual serology results if CDC is able to obtain CLIA approval for the assay?
 Yes No
5. May we contact you if we have any further questions?
 Yes No
If **YES**, Phone no: _____ Email: _____
6. Would you be willing to provide a follow up blood sample at a later time point if needed?
 Yes No Maybe
If **YES** or **MAYBE**, we will contact you in the future if we want to obtain blood samples.

Signature of participant _____ Date _____

Name of participant _____ Date _____

Name of person obtaining consent _____ Date _____

Signature of person obtaining consent _____ Date _____

COVID-19 Community Seroepidemiological Investigation

Parent/Guardian Consent for Minor 0-<18 years old

Assent additionally required for Children 7-17 years old

Individual ID# _____

The Centers for Disease Control and Prevention (CDC) is working together with Georgia Department of Public Health and Fulton and Dekalb Counties to learn more about the spread of COVID-19 (also called SARS-CoV-2) in communities.

To do this, we are talking to randomly selection households about COVID-19. We want to get a better idea of how many people in the community have been infected with SARS-CoV-2 (the virus that causes COVID-19), which will help the CDC and other public health officials make decisions about next steps in the response to COVID-19. Your house is one that has been randomly selected in your community.

We would like your child/ward to participate. Participation is entirely voluntary. If you agree to allow them to participate, we will conduct an interview with them or ask you to provide responses for their behalf for a child <7 years old using a standardized questionnaire. The questionnaire will collect information about your child/ward, including about their health. They/you can choose not to answer any questions that they/you might be uncomfortable with. We would also like to collect a blood sample from your child/ward to test for antibodies that would indicate past infection with SARS-CoV-2. This will not tell us if your child/ward is currently infected with SARS-CoV-2. The amount of blood collected will not exceed what is recommended for your child's weight and age. Risks of blood collection include discomfort with the needle stick, a small risk of bruising, redness or swelling around the site, a small risk of feeling lightheaded or fainting when the blood is drawn, and a rare risk of infection. There is no direct benefit to you or your child/ward from the blood draw, but your participation will help us learn more about COVID-19 and its spread in communities.

If you agree that your child/ward can participate, we will send your child's/ward's blood sample to the Centers for Disease Control and Prevention in Atlanta, GA for testing for antibodies to SARS-CoV-2. We will store what is left of the blood sample for other studies that we may do in the future related to the virus SARS-CoV-2. All your records, samples, test results, and interview answers collected for this investigation will be kept private.

The testing method for antibodies to SARS-CoV-2 is still being developed and is not yet an approved diagnostic test (CLIA approved test) as of 4/16/2020. CDC is working to obtain CLIA approval. CDC might get approval and if CLIA approval is obtained, individual serology results could be reported back to participants. The timeline for potentially being able to report results back is likely several months.

The results of these tests will help us understand how many people in a community have already been infected with SARS-CoV-2, which is important information to help public health officials make decisions about next steps in the response to COVID-19.

The participation of your child/ward in this investigation is voluntary, and you may withdraw your consent and decide at any time. The interview and blood draw are expected to take about 30 minutes per person. If you have any further questions, you may call (state/local jurisdiction/CDC) at xxx-xxx-xxxx.

For children aged 7 years or older, we will also be asking them for their assent to participate.

1. Have all of your questions about this public health investigation been answered?
 Yes No
2. Do you agree that your child/ward can be interviewed?
 Yes No
3. Do you agree that we can collect a blood sample from your child/ward?
 Yes No
4. Would you like to obtain your child’s individual serology results if CDC is able to obtain CLIA approval for the assay?
 Yes No
5. May we contact you if we have any further questions?
 Yes No
 If **YES**, Phone no: _____ Email: _____
6. Would you be willing for us to contact you in the future to request a follow up blood sample (if needed) from your child/ward?
 Yes No Maybe
 If **YES** or **MAYBE**, we will contact you in the future if we want to obtain blood samples.

Signature of parent/guardian Date

Name of parent/guardian Date

Assent of Minor ≥ 7 years old

I understand that this investigation is about SARS-CoV-2 (also called COVID-19). I understand that the interviewer will ask me questions about myself, including about my health, and that a blood sample will be taken. My questions have been answered, and I know that I can ask questions later if I have them.

- I agree to be interviewed Yes No
 I agree to have a blood sample taken Yes No

Signature of child/minor _____ Date

Print name of child/minor _____

Name of person obtaining consent/assent Date

Signature of person obtaining consent/assent

Date

Coronavirus disease 2019 (COVID-19) and you

What is coronavirus disease 2019?

Coronavirus disease 2019 (COVID-19) is a respiratory illness that can spread from person to person. The virus that causes COVID-19 is a novel coronavirus that was first identified during an investigation into an outbreak in Wuhan, China.

Can I get COVID-19?

Yes. COVID-19 is spreading from person to person in parts of the world. Risk of infection from the virus that causes COVID-19 is higher for people who are close contacts of someone known to have COVID-19, for example healthcare workers, or household members. Other people at higher risk for infection are those who live in or have recently been in an area with ongoing spread of COVID-19.

Learn more about places with ongoing spread at <https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html#geographic>.

The current list of global locations with cases of COVID-19 is available on CDC's web page at <https://www.cdc.gov/coronavirus/2019-ncov/locations-confirmed-cases.html>.

How does COVID-19 spread?

The virus that causes COVID-19 probably emerged from an animal source, but is now spreading from person to person. The virus is thought to spread mainly between people who are in close contact with one another (within about 6 feet) through respiratory droplets produced when an infected person coughs or sneezes. It also may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes, but this is not thought to be the main way the virus spreads. Learn what is known about the spread of newly emerged coronaviruses at <https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html>.

What are the symptoms of COVID-19?

Patients with COVID-19 have had mild to severe respiratory illness with symptoms of:

- fever
- cough
- shortness of breath

What are severe complications from this virus?

Some patients have pneumonia in both lungs, multi-organ failure and in some cases death.

People can help protect themselves from respiratory illness with everyday preventive actions.

- Avoid close contact with people who are sick.
- Avoid touching your eyes, nose, and mouth with unwashed hands.
- Wash your hands often with soap and water for at least 20 seconds. Use an alcohol-based hand sanitizer that contains at least 60% alcohol if soap and water are not available.

If you are sick, to keep from spreading respiratory illness to others, you should

- Stay home when you are sick.
- Cover your cough or sneeze with a tissue, then throw the tissue in the trash.
- Clean and disinfect frequently touched objects and surfaces.

What should I do if I recently traveled from an area with ongoing spread of COVID-19?

If you have traveled from an affected area, there may be restrictions on your movements for up to 2 weeks. If you develop symptoms during that period (fever, cough, trouble breathing), seek medical advice. Call the office of your health care provider before you go, and tell them about your travel and your symptoms. They will give you instructions on how to get care without exposing other people to your illness. While sick, avoid contact with people, don't go out and delay any travel to reduce the possibility of spreading illness to others.

Is there a vaccine?

There is currently no vaccine to protect against COVID-19. The best way to prevent infection is to take everyday preventive actions, like avoiding close contact with people who are sick and washing your hands often.

Is there a treatment?

There is no specific antiviral treatment for COVID-19. People with COVID-19 can seek medical care to help relieve symptoms.



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For more information: www.cdc.gov/COVID19