Community or clinic? Generating insights into COVID-19 transmission, severity, and response to vaccination with at-home antibody testing

Thom McDade, PhD
Northwestern University, Department of Anthropology and Institute for Policy Research
THE WORLD IS TEMPORARILY CLOSED
Screening for Coronavirus Antibodies in Neighborhoods (SCAN)

About the Study

The purpose of the SCAN Study is to find out how many people in specific areas have been exposed to SARS-CoV-2 (also known as coronavirus or COVID-19) and developed antibodies to the virus. The SCAN Study will also help researchers learn if these antibodies protect people against re-infection.

We will test your blood for antibodies to SARS-CoV-2, the virus that causes COVID-19. The timing of antibodies appearing in the blood stream is not fully known, some appear sooner than others, and some people develop antibodies without having symptoms of disease. We will test for antibodies, including those that can remain in the blood for a long time. In other types of infection, these antibodies often indicate immunity or a sign that the body has recovered from infection.

If you are interested in joining the SCAN Study, please answer a few questions in the form below to find out if you are eligible. Your responses are
An interdisciplinary research team

**Institute for Sexual and Gender Minority Health and Wellbeing (ISGMH)**
- Brian Mustanski
- Rana Saber
- Dan Ryan
- Melissa Mongrella
- Jack Novotny
- Krystal Madkins
- Reno Stephens
- Joshua Schrock
- Michael Newcomb

**Third Coast Center for AIDS Research (TC-CFAR)**
- Richard D’Aquila
- Nanette Benbow

**Department of Anthropology**
- Thomas McDade
- Aaron Miller
- Amelia Sancilio

**Center for Genetic Medicine**
- Elizabeth McNally
- Alexis Demonbreun
- Aaron Zelikovich
- Katherine Fallon
- Lauren Vaught
- Nina Reiser
- Jodi Curtain
- Matt Velez
- Ryan Hseih
- Lorenzo Pesce
The promise (and perils) of antibody testing

- Seroprevalence and the “denominator problem”
  - How many cases, where, whom?
- Evaluation of policies/behaviors that mitigate transmission in the community
- Origins of social inequities in COVID-19
  - asymptomatic vs. mild vs. serious infection
- Lasting effects of exposure/infection (Long COVID)

- Does antibody = immunity?
  - antibody “passports”
  - politics of seroprevalence
## Antibody testing in the community vs. the lab

<table>
<thead>
<tr>
<th>Community-based collection</th>
<th>QC/QA issues</th>
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<tbody>
<tr>
<td>Point-of-care</td>
<td>+</td>
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<tr>
<td>Finger stick</td>
<td>-</td>
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<tr>
<td>Rapid (&lt;15 min)</td>
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<td>HCW required</td>
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<td>Single test</td>
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</table>

**lateral flow immunoassay**

**Antibody Test, Seen as Key to Reopening Country, Does Not Yet Deliver**

The test, which made in China without FDA approval, can often inaccurate. Some doctors are withholding them. The vaccine is nowhere close to this demand.
Antibody testing in the community vs. the lab

**lateral flow immunoassay**

- Point-of-care
- Finger stick
- Rapid (<15 min)

**Community-based collection**

+ Qualitative
+ QC/QA issues
+ HCW required
+ Single test

- Quantitative
- Slow (3-5 hrs)
- Lab infrastructure

**Clinic-based collection**

- Travel to clinic
- Serum/plasma
- Collection materials
- PPE
- Licensed HCW

↑ accuracy
Retesting possible
"The filter paper blood collection device has achieved the same level of precision and reproducibility that analytical scientists and clinicians have come to expect from standard methods of collecting blood"  
Dried blood spots (DBS): Tool for bridging the field and the lab

Convenience and reach of community-based sampling + Accuracy and quantitation in the lab
Developing a DBS immunoassay for measuring SARS-CoV-2 antibodies
Permission to Take Part in a Human Research Study

Title of Research Study: Validation of immunosurveillance for SARS-CoV-2 antibodies

Investigator: Thomas McOdu

Supported By: This research is supported by Northwestern University.

Key Information:

We are asking you to fill out a short survey and provide a few drops of blood from a finger stick. These materials will be used to validate a new method for measuring exposure to coronavirus.

Why am I being asked to take part in this research study?

You are being asked to take part in this research study to help us understand more about the SARS-CoV-2 virus and how it affects the immune system. This information will be used to develop better ways to protect against the virus in the future.

What should I know about a research study?

- Someone will explain this research study to you.
- You can ask questions at any time.
- You can decide not to take part, or stop at any time.
- If you take part, you will not be harmed.
- Your decision will not affect your care.

Why is this research being done?

The purpose of this research is to better understand the immune response to SARS-CoV-2 and to develop new ways to monitor and prevent future outbreaks. This information will be used to improve public health strategies and to develop better treatments for COVID-19.
High seroprevalence for SARS-CoV-2 among household members of essential workers detected using a dried blood spot assay

A “no contact” approach to SARS-CoV-2 antibody testing.

Quantitative DBS assay for IgG antibodies

Web platform for participant engagement
Dried blot spot collection training material

Detailed inserts

Step by step video tutorials

Remaining questions: scan@northwestern.edu
No-contact research platform

1. **Online screener**
2. **Eligibility determination**
3. **eConsent + baseline survey**
   - Ineligible participants notified via email
4. **Waitlist**
5. **Test kits sent to ptps via USPS**
   - Automated email, SMS and voice call reminders
6. **Test kits returned by ptps with provided prepaid envelopes**
7. **Test kits processed and results are eReported to ptps**
SCAN substudies

SCAN Kids
SCAN Vaccine
SCAN Sensor
SCAN NUGENE
SCAN RADAR
SCAN FSM
SCAN Household
SCAN Chicago and Cook
SCAN ZIP
SCAN - Muscular Dystrophy
SCAN Kids - Muscular Dystrophy
Key findings

Origins of inequalities in COVID-19

One shot or two? Informing vaccination strategies

SCAN

Natural immunity and vaccine hesitancy
Pre-prints (peer-review is too slow!)
SCAN: 10 neighborhoods

Cumulative COVID-19 cases and ZIP code study areas

COVID-19 cases per 100,000 people, through April 30
- 1,076.1 to 1,358.4
- 834.3 to 1,076.0
- 644.5 to 834.2
- 394.9 to 644.4
- 68 to 394.8

Grouped by ZIP codes that will be compared in study:
- A: 60645: West Rogers Park
- B: 60660: Edgewater
- C: 60639: Belmont Cragin
- D: 60647: Logan Square
- E: 60612: Near West Side
- F: 60622: Ukrainian Village
- G: 60609: Back of the Yards
- H: 60615: Kenwood
- I: 60643: Beverly
- J: 60655: Mt. Greenwood

Sources:
- City of Chicago, Northwestern University, Chicago Tribune reporting
SCAN: 10 neighborhoods

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<th>housedx (%)</th>
<th>PCR+</th>
<th>Ab pos (%)</th>
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<td>0.00</td>
<td>0.17</td>
<td>0.73</td>
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</table>

Big differences in clinical cases across neighborhoods.

NO significant differences in seropositivity.
What explains the paradox of big differences in clinical cases vs. no differences in seropositivity?

Inequitable distribution of pre-existing health conditions
Higher “doses” of viral exposure

→ inequities in more severe COVID-19?
People Who Have Had Covid Should Get Single Vaccine Dose, Studies Suggest

New studies show that one shot of a vaccine can greatly amplify antibody levels in those who have recovered from the coronavirus.
Surrogate virus neutralization test (sVNT): Functional measure of antibody-mediated neutralization

In a BSL-3 lab...

- **live virus**
- **participant sample**

In a BSL-2 lab...

- **viral antigen**
- **participant sample**

ACE2 receptor

Neutralizing antibody

Spike protein

RBD of the spike protein binds to ACE2 receptor
Quantifying neutralizing antibodies (sVNT) in DBS

One shot or two? The answer depends on how you define prior exposure to SARS-CoV-2

Does durability of neutralization response vary by exposure history?

3 months post-second dose, by exposure history

- ~20% higher neutralization for COVID-19 cases in comparison with seronegatives AND seropositives
- Reduced neutralization of P.1 (Gamma) and B.1.351 (Beta) for all groups
- For seropositive/seronegative participants: Level of variant neutralization comparable to one dose mRNA

Natural immunity: Clinical vs. community-based perspectives

Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers


BACKGROUND
The relationship between the presence of antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the risk of subsequent reinfection remains unclear.

METHODS
We investigated the incidence of SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) in seropositive and seronegative health care workers attending testing of asymptomatic and symptomatic staff at Oxford University Hospitals in the United Kingdom. Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays, and staff members were followed for up to 31 weeks. We estimated the relative incidence of PCR-positive test results and new symptomatic infections according to antibody status, adjusting for age, participant-reported gender, and changes in incidence over time.

RESULTS
A total of 12,541 health care workers participated and had anti-spike IgG measured; 11,364 were followed up after negative antibody results and 1205 after positive results, including 88 in whom seroconversion occurred during follow-up. A total of 223 anti-spike-seronegative health care workers had a positive PCR test (1.09 per 30,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic, whereas 2 anti-spike-seropositive health care workers

ABSTRACT

The New England Journal of Medicine

ORIGINAL ARTICLE

Association of SARS-CoV-2 Seropositive Antibody Test With Risk of Future Infection

Raymond A. Harvey, MPH, Jeremy A. Rosen, ScD, Carly A. Kabela, BS, Wendy Turemire, MS, Sandy Leonard, MPH, Regna Kheir, MS, William A. Meyer III, PhD, DIABMM, MLS(ASCP), SC
Harvey W. Kaufman, MD, MBA; Steve Anderson, PhD; Oren Cohen, MD; Valentina M. Petrillo, MD, MPH
Kathy A. Crim, PhD, Allison L. Van Dyke, MD, PhD; Douglas R. Lowy, MD; Norman E. Sharpless, MD, Lynne T. Peabody, MS, MPH

IMPORTANCE
Understanding the effect of serum antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on susceptibility to infection is important for identifying at-risk populations and could have implications for vaccine deployment.

OBJECTIVE
The study purpose was to evaluate evidence of SARS-CoV-2 infection based on diagnostic nucleic acid amplification test (NAAT) among patients with positive vs negative test results for antibodies in an observational descriptive cohort study of clinical laboratory and linked claims data.

DESIGN, SETTING, AND PARTICIPANTS
The study created cohorts from a deidentified data set composed of commercial laboratory tests, medical and pharmacy claims, electronic health records, and hospital charges data. Participants were categorized as antibody positive or antibody-negative according to their first SARS-CoV-2 antibody test in the database.

MAIN OUTCOMES AND MEASURES
Primary end points were post-index diagnostic NAAT results, with infection defined as a positive diagnostic test post-index, measured in 30-day intervals (0-30, 31-60, 61-90, >90 days). Additional measures included demographic, geographic, and clinical characteristics at the time of the index antibody test, including recorded signs and symptoms or prior evidence of coronavirus 2019 (COVID) diagnoses or positive NAAT results and recorded comorbidities.

RESULTS
The cohort included 3,257,478 unique patients with an index antibody test. 54% were female with a median (SD) age of 48 (20) years. Of these, 2,876,771 (88.3%) had a negative index antibody result, and 378,606 (11.6%) had a positive index antibody result. Patients with a negative antibody test result were older than those with a positive result (mean age 48 vs 44 years). Of index-positive patients, 18.4% converted to seronegative over the follow-up period. During the follow-up periods, the ratio (95% CI) of positive NAAT results among individuals who had a positive antibody test at index vs those with a negative antibody test at index was 2.85 (95% CI, 2.73-2.97) at 0 to 30 days, 0.67 (95% CI, 0.61-0.74) at 31 to 60 days, 0.29 (95% CI, 0.24-0.35) at 61 to 90 days, and 0.30 (95% CI, 0.25-0.35) at more than 90 days.

CONCLUSIONS AND RELEVANCE
In this cohort study, patients with positive antibody test results were initially more likely to have positive NAAT results, consistent with prolonged RNA shedding, but became markedly less likely to have positive NAAT results over time, suggesting that seropositivity is associated with protection from infection. The duration of protection is unknown, and protection may wane over time.
Natural immunity: A justification for vaccine hesitancy

The Lancet Regional Health - Europe 1 (2021) 100012

Attitudes towards vaccines and intention to vaccinate against COVID-19: Implications for public health communications

Elise Paul, Andrew Steptoe, Daisy Fancourt

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<table>
<thead>
<tr>
<th>Variable</th>
<th>No, n = 279</th>
<th>Wait for Review, n = 1953</th>
<th>Yes, n = 1247</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>Do you think you are at risk of getting COVID-19 next year?</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001*</td>
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<tr>
<td>I believe I already have the disease and I am immune to it (Not diagnosed by a test)</td>
<td>30 (22%)</td>
<td>68 (49%)</td>
<td>40 (29%)</td>
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<tr>
<td>Yes, I am concerned that I will get mild symptoms which will probably not require hospitalization</td>
<td>153 (6.7%)</td>
<td>1283 (56%)</td>
<td>858 (37%)</td>
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<tr>
<td>Yes, I am concerned that I will get moderate symptoms which will probably need hospitalization</td>
<td>15 (2.6%)</td>
<td>350 (61%)</td>
<td>207 (36%)</td>
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</tr>
<tr>
<td>Yes, I am concerned that I will get severe symptoms which will probably require admission to the Intensive care unit</td>
<td>6 (3.4%)</td>
<td>106 (61%)</td>
<td>63 (36%)</td>
<td></td>
</tr>
</tbody>
</table>

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Vaccines 2021, 9, 119, https://doi.org/10.3390/vaccines9020119

Article

COVID-19 Vaccine Acceptance among Health Care Workers in the United States

Rahul Shekar 1, Abu Baker Sheikh 1,2, Shubhra Upadhyay 1, Mriganka Singh 2, Saket Kottewar 1, Hamza Mir 3, Eileen Barrett 1,3 and Suman Pal 1
Protective immunity: Clinical vs. community-based perspectives

Severity of infection

- Asymptomatic: 39.8%
- Symptomatic: 46.5%
- Clinical: 13.3%
- Hospitalized: 0.5%

McDade et al. (under review).
Protective immunity: Clinical vs. community-based perspectives

Prior infection ≠ protective immunity comparable to vaccination

McDade et al. (under review).
Cellular immunity to SARS-CoV-2

Neuro-COVID long-haulers exhibit broad dysfunction in T cell memory generation and responses to vaccination

Lavanya Visubbarathy1, Barbara Hanson1,3, Zachary Orban1, Patrick H. Lim1, Nicole Palacio2, Rishi Jain1, Eric Michael Liotta1, Pablo Penaloza-MacMaster2, Igor J. Korahnik4

C.

N pool stimulation

%Δ MIF CD4 T cells

Days post-symptom onset

p=0.11
R2=0.15

M pool stimulation

%Δ MIF CD4 T cells

Days post-symptom onset

p=0.45
R2=0.03

D.

N pool stimulation

%Δ MIF CD4 T cells

Days post-symptom onset

p=0.57
R2=0.07

M pool stimulation

%Δ MIF CD4 T cells

Days post-symptom onset

p=0.67
R2=0.09

Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection

Jennifer M. Day1,2, Jose Mateus1, Yu Kato1, Kathryn M. Hastie1, Esther Dawn Yu2, Caterina E. Faliti1, Alba Grifoni1, Sydney L. Ramirez2, Sonya Haupt2, April Frazier1, Catherine Nakao1, Vanseedhar Ravaprolu1, Stephen A. Rawlings1, Sjoerd Peters1, Florian Krammer1, Viviana Simon5,6, Erica Olmstead Saphire2,3, Davey M. Smith1, Daniela Wakes1, Alessandro Setta1,2, Shane Crotty1,2,4
Out of the lab and into the field:

Miniaturized cell culture protocols to advance research on the regulation of inflammation
Culturing cells is hard to do outside of the clinic. . .

. . . but not impossible.
Agreement in results across culture protocols

Community or clinic?

The vast majority of SARS-CoV-2 infections in the community are mild or asymptomatic, and do not generate high levels of protective immunity.

Scientific understandings of the immunobiology of SARS-CoV-2 are based primarily on the study of more severe cases of COVID-19 in the clinic.