



Collaborative
Cohort of Cohorts
for COVID-19 Research

Spring 2022
Participant Newsletter

Thank you from the C4R Investigators!

Dear C4R Participants,

On behalf of our entire research team, we would like to convey our gratitude for your incredible contributions to C4R, the **Collaborative Cohort of Cohorts for COVID-19 Research**.

For several reasons, C4R is recognized as a special and important resource to study risk and resilience factors for severe COVID-19 illness, “long COVID,” and other impacts of the pandemic. First, C4R includes a **diverse population of over 47,000 participants** from across the US. Second, thanks to their participation in long-term cohort studies, C4R participants have detailed information on their pre-COVID heart, lung, and brain health. **C4R is investigating how these pre-COVID health conditions may be related to short- and long-term health effects of COVID-19.** In this way, C4R will be able to answer important questions that may be difficult to address in other studies.

Research is not possible without participants like you, and we are privileged to have your support of this important NIH-funded COVID-19 research initiative. In this newsletter, you will find information on the goals of C4R, ongoing work, FAQs, and preliminary findings. We look forward to providing you with more updates in the coming months.

Sincerely,

The C4R Research Team

www.c4r-nih.org



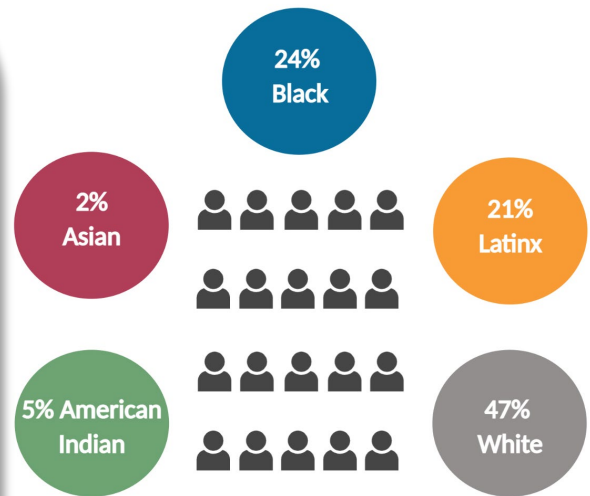


What is C4R?

A cohort study allows researchers to follow participants over a period of time—often over many years. The Collaborative Cohort of Cohorts for COVID-19 Research, or ‘C4R’, brings together 14 cohort studies funded by NIH that have been following participants across the US for up to 50 years.

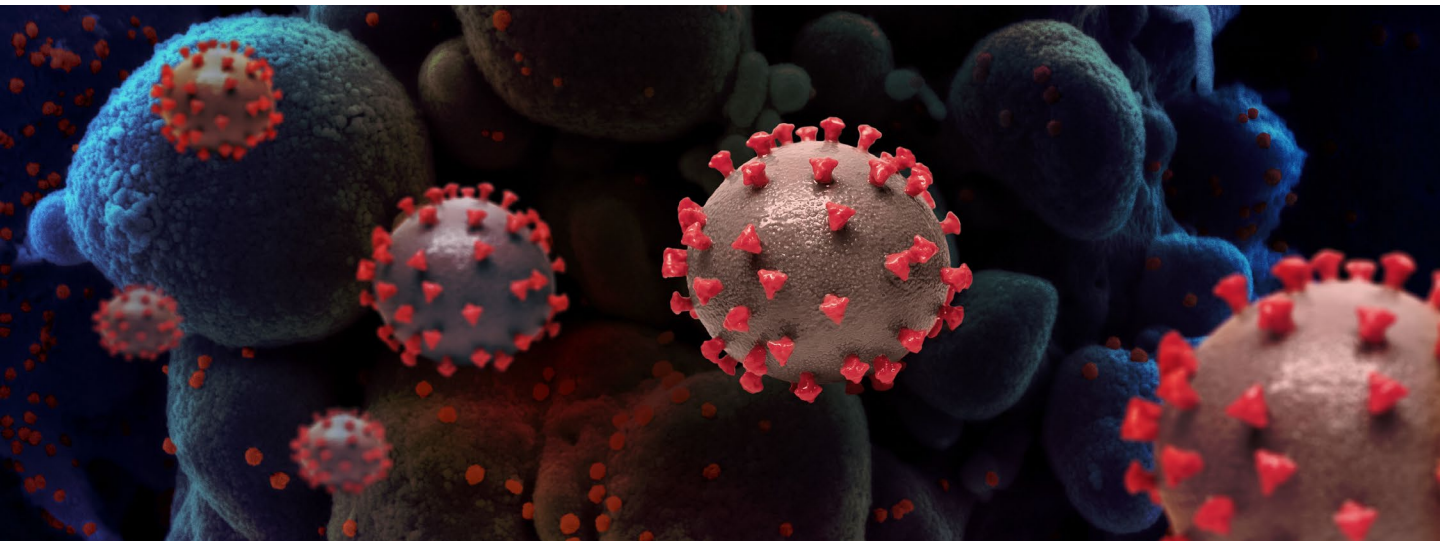
Who is participating in C4R?

C4R includes a diverse population of **47,000 participants from 14 cohorts and nearly every U.S. state**. Our 14 cohorts include: ARIC, CARDIA, COPDGene, PrePF, Framingham Heart Study, HCHS/SOL, Jackson Heart Study, MASALA, MESA, NOMAS, REGARDS, SARP, SPIROMICS, and the Strong Heart Study.



Created with BioRender.com

C4R is diverse and includes many participants from different race and ethnic groups



What are the goals of C4R?

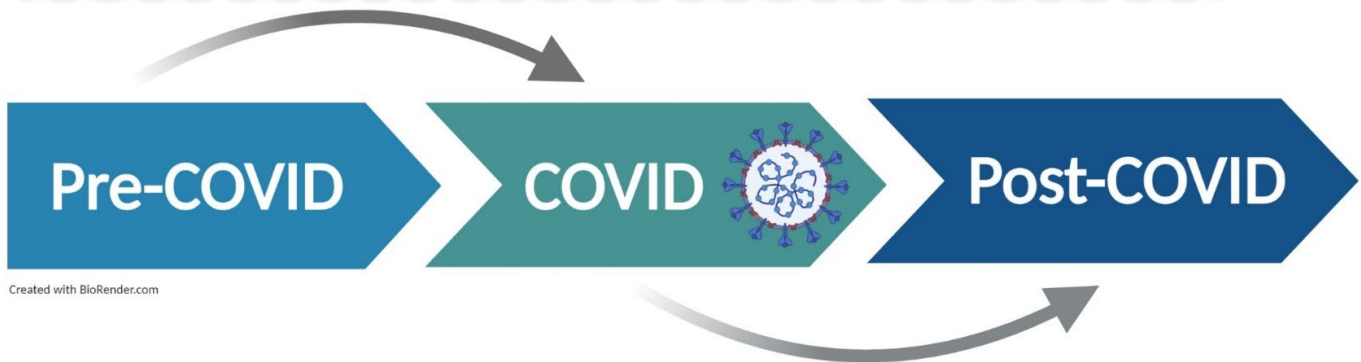
C4R aims to study risk and resilience factors for:

- Severe COVID-19 illness
- “Long COVID”
- Other pandemic health effects

Our goal is to understand what increases or decreases the likelihood of developing severe or prolonged COVID-19 illness.

What are the key research questions?

How do pre-existing health conditions affect risk of severe or prolonged COVID-related illness?



How do SARS-CoV-2 infection and COVID-19 illness affect long-term health?

How has the pandemic affected health-related behaviors and non-COVID health outcomes?

Questionnaires



- **47,699** participants have completed at least one C4R questionnaire
- The questionnaire asks about COVID-19 testing, infection, hospitalization, and other pandemic-related experiences.

COVID-19 Related Health Outcomes

As of February 2022, the number of C4R participants with personal experiences of COVID-19 is as follows, with higher rates of COVID-19 infection with obesity, high blood pressure, diabetes, and smoking. C4R is committed to understanding the factors that contribute to these disparities so that they can be addressed.

6,564
self-reported
infections



4,180
test positives

988 non-fatal
hospitalizations



375 COVID-
related deaths

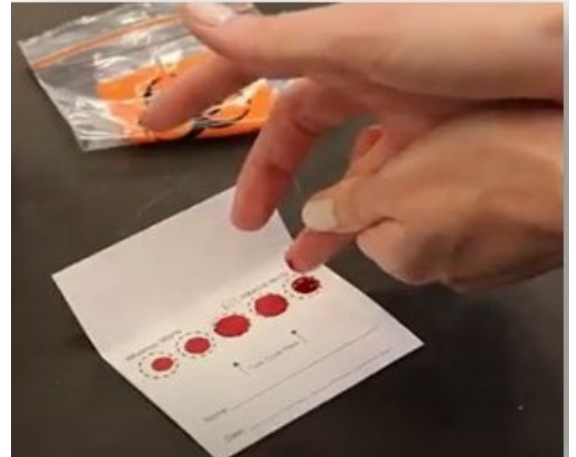
12,482 reactive
serology results



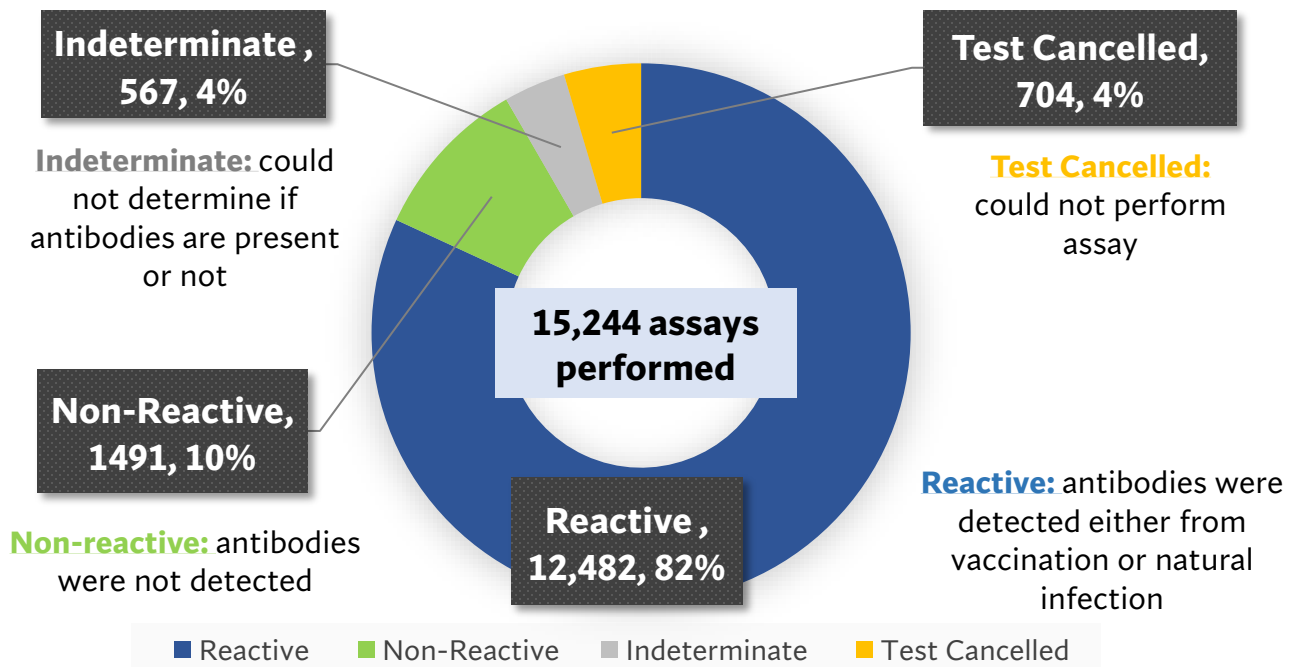
1,491 non-reactive
serology results

Dried Blood Spot (DBS) Collection

- **15,722** participants have returned a finger-prick sample of blood via a DBS card
- **15,244** of these samples have been tested for evidence of antibodies to the virus that causes COVID-19 – see below for more details!



Serosurvey for SARS-CoV-2 Antibodies



C4R Researchers can use specific antibody data to assess whether your DBS result is reactive due to natural infection, and *potentially* which variant caused the infection.



Frequently Asked Questions (FAQs)

If I have antibodies against SARS-CoV-2, what does it mean?

If you received a result saying that **antibodies were detected on your dried blood spot for C4R (a “positive” test)**, this means you may have been vaccinated for COVID-19 or it could also indicate you have antibodies from an infection with the virus that causes COVID-19. Please note that this does not necessarily mean that you are protected from COVID-19 in the future. It also does not mean that you have the virus now or might infect other people.

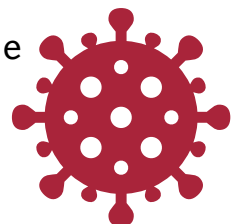
If I do not have antibodies against SARS-CoV-2, what does it mean?

If you received a result saying that **antibodies were not detected on your dried blood spot for C4R (a “negative” test)**, this tells that you did not have a high level of antibodies at the time you gave us your blood sample, although you could still have some antibodies. Antibodies can take several weeks to develop and then antibodies decrease over time, eventually reaching a level so low that they might not be detectable.

Will you be able to tell me if I have antibodies from an infection versus from vaccination?

As a participant, you will not receive information on whether your antibodies, if present, are likely to be due to natural infection and/or vaccination. There are rules governing the types of information we can share with participants, and therefore **we will only be able to tell you if you do or do not have evidence of antibodies to SARS-CoV-2 in your bloodspot.**

Nonetheless, C4R will be able study whether your blood spot has antibodies to the “Spike” or “S” protein and/or to the “Nucleocapsid” or “N” protein as part of our research. This helps us understand whether your antibodies are from natural infection or vaccination. When you are infected with SARS-CoV-2, your body is likely to make antibodies to both S and N proteins. By contrast, the vaccine will only train your immune system to make antibodies to the S protein. Again, unfortunately we will not be able to share these details on S and N antibodies with you directly, but it will greatly contribute to our scientific investigations.



Some questions we will answer with C4R...

- Does COVID-19 increase the long-term risk of major health events such as heart attack, heart failure, kidney failure, or stroke? Do we also see more of these health events than we would expect in non-infected adults and, if so, can we understand why?
- Does COVID-19 result in an increased risk of conditions like diabetes, or does it just lead to more new diagnoses?
- What is “long COVID”? Is there such a thing as asymptomatic “long COVID”?
- What are the features of infection versus reinfection?
- Who gets the most benefit from COVID vaccine “boosters”?
- What is the antibody response to the vaccine(s) vs different COVID-19 variants?
- Does SARS-CoV-2 infection accelerate cognitive decline in older adults?
- What has been the impact of COVID infection and the pandemic itself on mental health across different US communities?
- Beyond vaccines, are there medicines or behaviors that reduce risk of severe COVID-19, long COVID, or other adverse pandemic effects?

There are currently 40+ proposals underway to address COVID-19 research questions using C4R data!

Below are some of the domains under investigation:



Neurocognition
Brain MRI



Biomarkers
DBS
Hematology



Genomics



Lung CT



Geocoding



Vaccination



Harmonization



Cardiovascular



Statistics



Tobacco



Social Determinants
of Health

And many more!



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How do I learn more about C4R?

Visit our website: www.c4r-nih.org
and follow us on twitter @C4RStudy!

