

SIREN

SARS-CoV2 Immunity & Reinfection Evaluation

SIREN Participants Newsletter
Issue 2
Aug 2021

Dear SIREN participants,

Welcome the second issue of the SIREN study Participants' Newsletter!

As you may be aware, on the 18th of June, the SIREN study celebrated its **first anniversary**, and it has been a year of outstanding achievements. We would like to thank you all for your support and contributions, without which none of these would have been possible.

Thanks to your collaboration, we have learnt that *reinfections may happen, but they are rare events*. In our [first published study](#), the risk of someone getting *COVID for a second time* was 84% lower than someone who had never had the disease. However, in this study, we only had the chance to analyse the data you provided to us from June 2020 to January 2021, including participants who were not vaccinated. The next questions we are looking forward to answering include: how long are you protected from SARS-CoV-2 infection after a previous infection and vaccination? And how will your antibody response behave in the long run?

With the COVID-19 vaccine roll-out, we also started to investigate how effective vaccines are in real life. We published [one study on the Pfizer vaccine](#) and concluded that *one dose of this vaccine reduced the risk of getting infected with SARS-CoV-2 by 70%*, compared to those who had not been vaccinated. *After the second dose, protection was even higher, with an 85% reduced risk of infection*. We are currently performing the same analysis for the AstraZeneca vaccine, and results will be published soon.

To celebrate and thank you for your support, we would like to share with you this [anniversary message from Dr Susan Hopkins and Professor Chris Whitty](#).

Save the date: SIREN Participants live event + Q&A Thursday 16th September 16:00-17:00

We would like to invite you to the next SIREN Participants live event in September when we will be able to share some of our recent findings, keep you updated on study changes and most importantly answer your questions. We look forward to seeing as many of you as possible on the 16th September.

Add this to your calendar and [click here](#) to join the live event on MS Teams.

We look forward to seeing you then.

Option to extend SIREN follow-up

Following positive feedback from both sites and participants, we are delighted to confirm that we have submitted a protocol amendment to extend SIREN for up to an additional 12 months. This has been accepted by Research Ethics Committee (REC), and we are currently consulting sites whether they would like to offer the extension. If your site agrees, then towards the end of your 12-month follow-up you will be offered the opportunity to continue your involvement in SIREN for up to a further 12-months.

We now have a number of sites offering the extension and we would like to thank all the participants at those sites who have opted to join the extended follow-up so far. We have had a really positive response from participants offered the chance to extend their follow-up to date. So far, in the sites that have already started running the extension, we have received great feedback from participants, with 90% of those who have submitted the survey opting into the extension.

Why is a follow-up extension important?

This extended follow-up is critical for us to study the duration of immune response following infection and vaccination at longer intervals. If you currently have immunity from COVID-19, it may be an opportunity to find out how long this protection lasts. In addition, we will be able to detect and investigate infections following vaccination and understand why this happens. Working together we will be able to continue to provide critical information to inform national policy-making on COVID-19.

There are still many questions we would like to answer, such as:

- What are the chances of someone getting COVID after one or two doses of vaccine?
- How will our antibodies behave after vaccination? Is it similar to when you are infected by the virus?
- Are two doses of vaccine enough? Will we need to be re-vaccinated after a period?
- How long does immunity from vaccines last? Does it differ depending on the vaccine?

These are just a few questions that we are working on, and to address them, your continued contribution is essential. With the extension and your support, we will be able to follow you up for another year and develop robust data to better understand the immune response against COVID-19.

No action is required from you at present, but please be aware that if you are a participant at a site offering the extension you may expect further communication from us and your local SIREN team in the future with more information about the options for extending follow-up after 12 months.

Funding awarded to investigate immunity following vaccination

We are delighted to report that the SIREN study, together with academic partners, has recently been awarded a major grant from a UK research funding body to investigate immunity after vaccination. There will be a formal announcement in the coming weeks.

We will be working with leading immunologists and scientists to investigate infections after vaccination and to study the long-term immune response to vaccines. This is a prestigious and competitive award and it is a testament to the value that the wider scientific community place on the data that your participation has provided. We are very excited to be embarking on this phase of the study and hope that many of you will be able to join us in the planned extension of the study to support these endeavours.

Frequently asked questions about antibodies against SARS-CoV-2

Antibody tests detect antibodies produced by your body after natural infection or vaccination.

But what are antibodies? An antibody is a protein produced by the body's immune system when it detects harmful substances called antigens.

Currently, there are two types of antibody tests for COVID-19:

- **Spike (S) protein** – This test checks if you have antibodies against the spike protein of the virus – a protein located on the exterior part of the coronavirus
- **Nucleocapsid (N) protein** - This test verifies if you have antibodies against the nucleocapsid protein of the virus – this protein is located in the inner part of the coronavirus together with virus genetic material.

When someone is infected by the coronavirus (natural infection), they have contact with all the parts of the virus, i.e. 'S' and 'N' proteins. This means that, when this person is tested for antibodies, it is expected they will be positive for both proteins. On the other hand, vaccinated people who have never been infected by the virus will only produce antibodies against the S protein. This happens because COVID-19 vaccines inject parts of the virus that will trigger our immune response only against the S protein.

Following this brief explanation, it is easier to answer some of the frequent questions.

1. Why my antibody test is negative if I have been vaccinated against COVID-19?

There are a number of reasons to why this may be happening:

- a. Time:** usually antibody tests become positive after 2-6 weeks of natural infection or vaccination. Please allow for a few weeks after you got vaccinated for any antibodies to be detected with an antibody assay.
- b. Type of antibody test:** Your site may not be using an antibody test that detects antibodies produced after vaccination (i.e. they are testing for antibodies against infection - N protein).
- c. Limitation of the test:** your antibody levels are at very low levels that current the antibody test cannot detect.
- d. Individual immune response:** you may be one of a small percentage of people who do not develop antibodies following infection or vaccination.

It is important to remember that a negative antibody test following infection or vaccination does not mean you are not protected from COVID-19, as we know that there are different immune protection responses to COVID-19. The association between antibodies and protection is one of the themes that SIREN is studying, and your role in the study is essential.

2. I have detectable antibodies. How do I know if my antibodies are due to the vaccine or a previous natural infection?

This depends on what antibody testing is available at your site. If your test is positive to the nucleocapsid protein (N): this is a marker of past infection. If your test is positive to the spike protein (S): this could be the result of either previous infection or vaccination. If you have only been tested after vaccination, then it will not be possible to work this out based on testing available to you at your site

Thank you!

We really appreciate your contribution so far and hope you continue to participate in SIREN, so we can come out of this pandemic stronger. **Thank you for making SIREN happen!**

All the best,
The SIREN team at PHE