

SIREN

SARS-CoV2 Immunity & Reinfection Evaluation

SIREN Participant Webinar 29 April 2021 Frequently Asked Questions

Thank you everyone for participating in SIREN, and to all the many hundreds of you who joined us in the second SIREN participants webinar on 29th April 2021. Recruitment in SIREN ended on 31st March 2021 with over 44,000 participants enrolled, making us the largest healthcare worker cohort study on SARS-CoV-2 in the world! In this document, we address the main questions that were raised and discussed in this webinar. We look forward to your participation in our future SIREN participant webinars.

1. I have been vaccinated against COVID-19 but I do not have antibodies. Is this normal?

Please allow for a few weeks after you got vaccinated for any antibodies to be detected with an antibody assay. If more than a few weeks have passed since vaccination and your antibody test returns negative, there are a couple of reasons why this might be happening. It might be that your site is not using an antibody test that detects antibodies produced after vaccination (antibodies to the spike (S) protein) and therefore is unable to measure your antibody response to vaccination. You can check with your site which antibody assay they use. If your site is using the antibody test that detects antibodies following vaccination, but you are negative after vaccination, this could be because your antibody levels are at very low levels that current antibody tests cannot detect. Alternatively, you may be one of a small percentage of people do not develop antibodies following vaccination. It is important to remember that a negative antibody test following vaccination does not mean you are not protected from COVID-19, as we know that there are different immune protection responses to COVID-19. We will continue to look at these as part of SIREN.

2. Is there any scope for testing using the assay that detects antibodies against the spike protein in SIREN?

Antibody assays used vary among SIREN sites, and decisions about which antibody test is in use locally is the responsibility of the site. We are aware that there is interest to get post-vaccination antibody testing among some SIREN participants at sites at which this is not available and are actively investigating how we can support this. We will keep you updated on this.

3. 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 site tests for antibodies to the nucleocapsid protein (N), this is a marker of past infection. If you are positive on this test, then you are likely to have had COVID-19 in the past. If your site targets the spike protein (S) and you are positive, then this could be the result of either previous infection or vaccination, as S-antibodies are produced in response to both natural infection and vaccination. Interpreting your result will depend on the timing of your antibody test in relation to vaccination. If you were positive on an S-antibody assay before you were vaccinated, then this means you had antibodies following natural infection. 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.

4. Are antibodies after a natural infection more effective against COVID-19 than antibodies following the vaccine?

The answer to this is currently unknown, and it is an important question driving current research, including within SIREN. The SARS-CoV-2 virus has a few parts of it that are recognised by the immune system and trigger a response. We know that there are some differences in the immune response that can be detected after natural infection and vaccination. Importantly, antibodies can wane with time and vaccines can act as boosters of immunity even among those who have had a natural infection. This is why vaccination is recommended for most adults, including those who have had infection in the past. SIREN will provide key data to answer this question, by analysing your antibody response over time. This will only be possible by you continuing to provide serum samples over time, so please do continue to attend your follow-up appointments!

5. Will I receive the results of testing conducted by PHE on my serum samples?

You should be kept informed of the results of your local PCR and antibody testing within SIREN by your site according to your site's procedures. Within SIREN we collect and store (biobank) serum from all participant baseline visits, and from follow-up visits for participants who have ever been infected or vaccinated. It is important to note that we do not run every test on every sample at the PHE laboratory. Samples are tested for specific analyses, for example to investigate cases of reinfection, or measure antibody response following vaccination. We are aware that some participants would like to receive the results of this PHE testing and we are investigating how this may be possible in the future.

6. Is T-cell immunity more effective than antibodies against COVID-19?

This is another unanswered question, which is the focus of current research efforts, including within the SIREN-associated Protective Immunity from T Cells in Healthcare Workers (PITCH) study. T cells are another important component of the immune response, distinct from antibodies. A number of SIREN participants, at sites in Liverpool, Newcastle and Sheffield are co-enrolled in PITCH. SIREN participants who experience reinfection or infection after vaccination may also be approached to join PITCH, to understand more about their T cell response. If you are one of these participants, thank you for your contribution to these two important studies!

7. Why did I receive a recent communication from NHS Test & Trace asking me to share my negative SARS-CoV-2 test results with the COVID-19 app?

We are aware that a small number of SIREN participants in England received a communication from NHS Test & Trace (NHS T&T) in April 2021, asking them to record their COVID result in the NHS COVID-19 app. We have now worked with NHS Test and Trace to ensure that you should only receive a request to record your test result in the NHS COVID-19 App if you test positive at any point.

We would like to take this opportunity to explain that all SARS-CoV-2 PCR and antibody test results (both negative and positive) are notifiable as a matter of course to your national public health agency (either Public Health England, Public Health Scotland, Public Health Wales or Health and Social Care Northern Ireland). In England, NHS T&T are legally notified of all PCR results, both in and outside of SIREN and participants did not receive this communication because they were part of SIREN. We would like to reassure you that we take the protection of your personal information very seriously and only ever share your information where it is lawful and justified for us to do so.

8. Is my participation in the study still useful?

YES! We have a number of important research questions that we are actively working on. For example, we are trying to assess how long antibody levels remain detectable for, following a natural infection or vaccination. We are also trying to assess how vaccines work and how effective they are in protecting against future infections. Your participation in SIREN, regardless of your professional circumstances (e.g. midwives, porters, security staff, nurses, medics, administration staff), directly informed the national path out of the lockdown. Being the largest cohort of its kind in the world, the SIREN study is expected to continue informing national policy. The longer you participate, the more valuable results we will be able to produce!

9. Is there evidence that the vaccines offer protection against variants of concern?

This is a current priority question for the international scientific and public health community, particularly with the emergence of new variants. SIREN has an important contribution to make here. Detailed analysis on your positive PCRs within SIREN will allow us to identify variants of concern and how vaccines are effective against it, after combining this with data on your vaccine status.

10. Is the duration of SIREN likely to be extended?

We have been delighted with the feedback that so many participants are keen to continue with SIREN after their 12-month follow-up. There are still so many critical questions that SIREN can help to answer, from long-term effectiveness of the vaccines to questions on variants of concern. We are therefore actively looking into ways to extend SIREN beyond the original 12-month follow up for people who wish to remain involved, in a more flexible format. Although we don't have any definitive answers at the moment, we hope to have more information soon.