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# SIREN PARTICIPANT NEWSLETTER

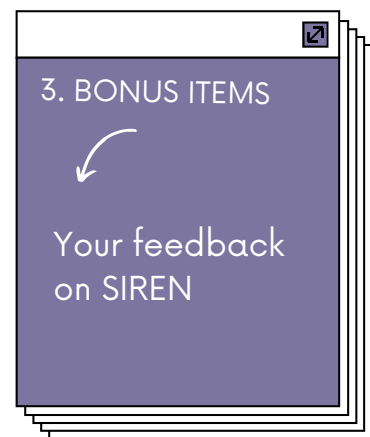
21 APRIL 2023

**Dear colleagues,**

Welcome to the latest issue of the SIREN newsletter. We have included some key study updates below and will keep you informed on future steps once we have further information.

In this edition we are excited to share our recent research outputs from SIREN.

As always we welcome your feedback and encourage you to reach out with any questions or suggestions, either through filling out the form on [this link](#) or contacting us via our dedicated inbox at [phe.siren.participants@ukhsa.gov.uk](mailto:phe.siren.participants@ukhsa.gov.uk).





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## 1. Announcements

### A) New research from SIREN: Correlates of protection following COVID-19 vaccination

A new SIREN study pre-print has just been published looking at antibody immunity to COVID-19 in vaccinated compared to unvaccinated SIREN participants. This is a preprint meaning the analysis, results and interpretations will be fine tuned during the peer review process. We think this is an important contribution to our understanding of COVID vaccines and so are sharing now. Thank you again for making this possible.

#### Preprints with THE LANCET

Preprints with The Lancet is part of SSRN's First Look, a place where journals identify content of interest prior to publication. Authors have opted in at submission to The Lancet family of journals to post their preprints on Preprints with The Lancet. The usual SSRN checks and a Lancet-specific check for appropriateness and transparency have been applied. Preprints available here are not Lancet publications or necessarily under review with a Lancet journal. These preprints are early stage research papers that have not been peer-reviewed. The findings should not be used for clinical or public health decision making and should not be presented to a lay audience without highlighting that they are preliminary and have not been peer-reviewed. For more information on this collaboration, see the comments published in The Lancet about the [trial](#) period, and our decision to make this a [permanent](#) offering, or visit The Lancet's [FAQ](#) page, and for any feedback please contact [preprints@lancet.com](mailto:preprints@lancet.com).

#### Antibody Correlates of Protection Against Delta Infection after Vaccination: A Nested Case-Control within the UK-Based Siren Study

23 Pages • Posted: 18 Apr 2023

[Ana Atti](#)  
Public Health England Colindale

[Ferdinando Insalata](#)  
UK Health Security Agency

[More...](#)

#### **Abstract**

Background: Identifying numerical correlates of protection (CoP) against SARS-CoV-2 infection remains critical for public health strategy. Nested within SIREN, a UK-based large cohort study, we investigated serological CoP against SARS-CoV-2 B.1.617.2 (Delta) infection after two vaccinations.

Methods: We performed a case-control study, where cases were Delta infections after second vaccine dose and controls were vaccinated, never infected participants, matched by age, gender and region. Sera were tested for anti-SARS-CoV-2 Spike antibodies levels (anti-S) and neutralising antibody titres (nAbT), using live virus microneutralisation against Ancestral, Delta and Omicron (BA.1, B.1.1.529). We modelled the decay of



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## Overview

This research looks at whether vaccinated people who were infected with Delta variant after their second dose produce a different immune response compared to vaccinated people who were never infected with COVID-19. We also investigated whether a protection threshold could be numerically defined based on antibody results. This is also known as serological correlates of protection (CoP).

## What is a correlate of protection?

A CoP is something you can measure in the lab that predicts immunity from a disease, either from a vaccine or natural infection. You could measure blood, serum or saliva and a CoP could be determined using assays that detect either antibodies or specific blood cells (called T-cells). In this study, we investigated correlates of protection using blood tests for antibodies. Hepatitis B and Rubella are clinical examples that test antibodies as a correlate of protection.

## Why are correlates of protection important?

The aim of measuring CoP is to understand the level at which a person can fight off a future infection (such as COVID-19). If you have a numerical value for a CoP, you could use this to:

- Plan for future booster vaccination doses
- Identify vulnerable groups
- Inform interventions for infection control at a populational level



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## What question does this research aim to answer?

Could a numerical threshold for a CoP against Delta infection be determined?

## How was the study performed?

The study looked at healthcare workers in the SIREN study who had received 2 doses of the COVID-19 AZ vaccine. They were split into two groups:

- 130 participants with a PCR confirmed COVID-19 infection caused by Delta variant after their second vaccine dose (cases).
- 318 participants who were never infected before or after their second vaccine dose (controls).

COVID-19 antibody levels were measured for both groups, in several data points, but focusing on samples after vaccination and before infection for cases and similar calendar time samples for controls, to assess if there were any differences between groups. We also looked at antibody waning after the second vaccine dose.

For this, we have performed different antibody test in these samples:

- Anti-S, which is total amount of antibodies conferred by vaccination, in this case
- Neutralising antibodies, which are specific antibodies that are able to neutralise the SARS-CoV-2 virus and unable them to cause infection



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## What were the main results?

- Cases had lower levels of anti-S and neutralising antibodies when compared to controls.
- Anti-S antibodies correlate less with protection against infection than neutralising antibodies.
- Participants with detectable neutralising antibodies (>40) at 7 days before infection with the Delta variant had a 89% reduction in odds of infection compared to those with lower antibody levels.
- There was an additional benefit for higher antibody titre levels.
- A correlate of protection against COVID-19 infection was therefore identified for Delta infection after 2 doses of vaccination.

## What are the implications of this?

This study demonstrated that Delta neutralising antibody titres correlate strongly with infection against COVID-19 Delta infection. We have shown there is a numerical threshold around which the risk of COVID-19 infection can be measured at population level, which has implications for vaccine deployment and public health measures around COVID-19.

**[Read the full pre-print here](#)**



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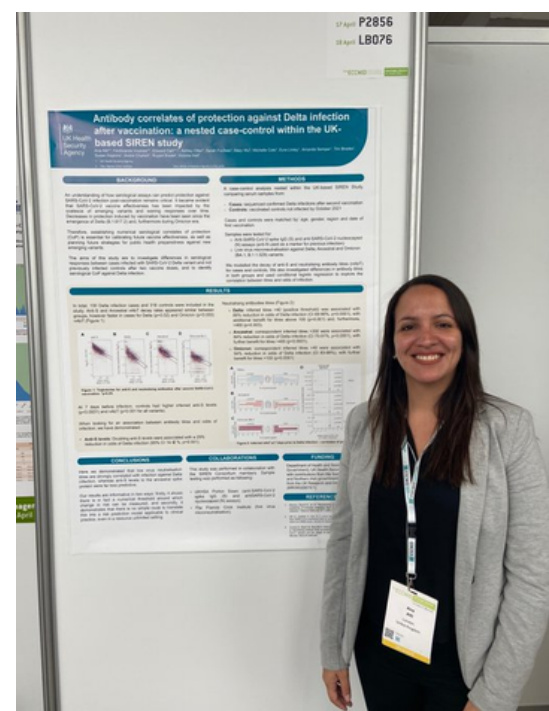
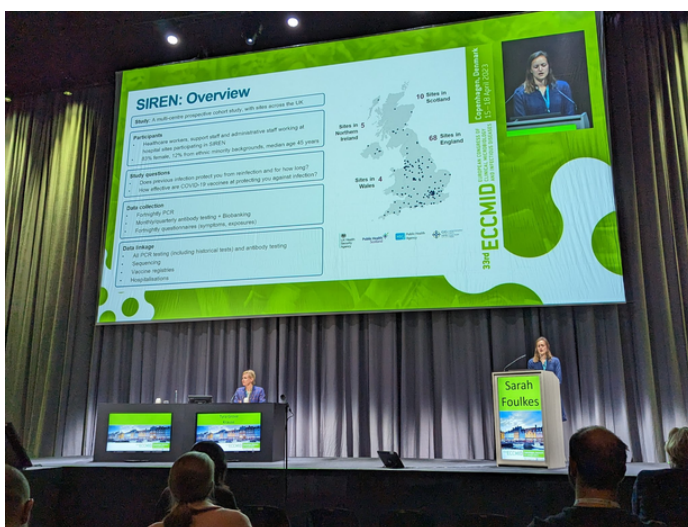
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## 2. SIREN in the spotlight

### A) The SIREN team at ECCMID Congress 2023

This year we were delighted to share research outputs from SIREN at the European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) in Copenhagen. The team delivered talks on how SIREN has developed our understanding on vaccine effectiveness and the impact of prior COVID-19 infection on immunity, influenza vaccination coverage within the cohort, our successful winter pressures pathway investigating additional respiratory viruses in our cohort, and our qualitative research workstream including the crucial role of participant involvement in SIREN.

Many thanks for your ongoing contributions to this important study which receives significant visibility in the international research community, and congratulations to the team for their presentations!

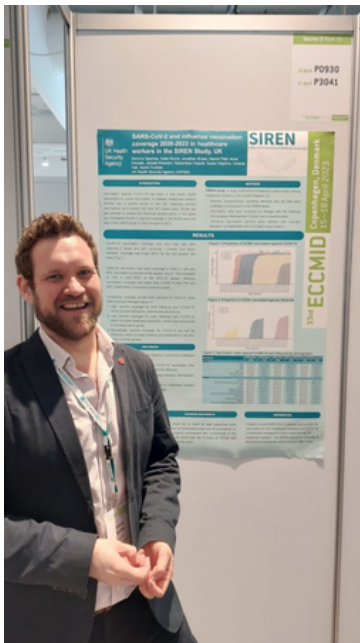




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## B) SIREN featured in NCSi impact report



The National Core Studies (NCS) Immunity Programme set out its new impact report today. NCS Immunity was one of six National Core Studies and aims to deepen our understanding of immunity against COVID-19, how to use vaccines most effectively, and how to prepare for future pandemics. The SIREN study features in this report which can be accessed [here](#):

*"The SIREN study used regular samples from nearly 45,000 healthcare workers to monitor COVID-19 infections across the UK. In two years, it carried out over a million PCR tests and more than 400,000 blood tests. SIREN has helped shaped our understanding of COVID-19 infections, reinfections and the protection offered by vaccines. The study also played an important role in national surveillance, offering insight into infection trends and monitoring emerging COVID-19 variants."*



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## 3. Bonus items

### A) Your feedback on SIREN

SIREN is shaped by your feedback. We have loved hearing your experiences of being part of the SIREN community:

"I felt it was very important to be part of this research and so much has been learned through this. I was really pleased that I was able to sign up for this research programme."

**Patricia Beard,  
St George's  
Hospital Trust**

"I felt it was a really important study to help inform scientists on how to deal with the COVID-19 pandemic"

**Julie Lynch, LTHT**

"The Devon Partnership Trust SIREN team have worked tirelessly on ensuring the study runs effectively. I feel incredibly proud and feel we have really contributed to learning about the COVID-19 pandemic through research"

**Natalie Crooks, Devon  
Partnership Trust**



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Please continue to share your reflections and experiences of being part of SIREN using [this link](#).



## Sharing stories: reflections and stories from SIREN sites and participants

SIREN is shaped by your feedback and case studies are a key part of that.

Please submit your reflections below to be featured in a future issue of the SIREN newsletter.

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Please use the space below to share your reflections on the SIREN study. For SIREN 1. sites, please feel free to use the space below to share more about initiatives or achievements at your site.

Enter your answer