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Does the presence of antibodies to SARS-CoV-2 reduce the risk of subsequent COVID-19 in healthcare workers?

Submission date
04/01/2021

Recruitment status
No longer recruiting

Registration date
12/01/2021

Overall study status
Ongoing

Last Edited
04/07/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.

In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.

Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.

Understanding people's immunity to COVID-19 is key to controlling the virus and informing how we deal with potential future waves. SIREN is investigating whether people can be re-infected by the SARS-CoV-2 virus that causes COVID-19 and therefore if someone can catch COVID-19 more than once.

The aim is to find out whether healthcare workers test positive for COVID-19 more than once, or whether they test positive for COVID-19 even though they have some immunity.

Who can participate?
Healthcare workers aged 18 years or older, who work with patients in a clinical setting can take part

What does the study involve?
When someone joins the study they provide a blood sample and a nose and throat swab. The blood sample tests for antibodies, which indicate someone has some immunity to COVID-19, and the nose and throat swab tests for the virus. These two tests indicate whether someone has ever had COVID-19 (a positive blood test), or whether they have it right now (a positive nose and throat swab).
Every two weeks, healthcare workers will do a nose and throat swab and complete a questionnaire about any exposure to the virus and any symptoms they have. Every four weeks a blood sample will be taken to test whether they have any immunity. Participants will be followed for one year and may be asked to provide extra samples, if additional tests are needed to determine whether they may have been re-infected.

What are the possible benefits and risks of participating?
The study will not benefit participants directly but will help provide important information about SARS-CoV2 re-infection among staff working in healthcare organisations and provide a stronger evidence base to inform national guidance and policy.

For some, blood sampling may cause momentary discomfort at the site of the blood draw, possible bruising, redness, and swelling around the site, bleeding at the site, feeling of lightheadedness when the blood is drawn, and rarely, an infection at the site of blood draw. Some individuals may find the swab tests uncomfortable. The study is following ethical guidance to ensure that the volume of blood taken is within safe limits.

Where is the study run from?
Current as of 06/12/2022:
The UK Health Security Agency (UKHSA) runs the SIREN study in partnership with the Public Health Agency Northern Ireland, Public Health Scotland, Public Health Wales and NHS sites. A total of 135 NHS Trusts have participated in the study involving almost 45,000 participants, making SIREN the largest study of its kind globally. The SIREN study also collaborates with a number of academic partners.
Previous: The study is run by Public Health England in collaboration with a number of Universities. Over 100 NHS Trusts are participating in the study, which is where samples are taken.

When is the study starting and how long is it expected to run for?
May 2020 to March 2028

Who is funding the study?
Current as of 06/12/2022:
The SIREN Consortium was established in August 2021 and was successfully awarded a £1.57 million research grant by UK Research and Innovation (UKRI).
Previous: The Department for Health and Social Care (UK)

Who is the main contact?
Prof Susan Hopkins, siren@ukhsa.gov.uk

Study website
https://www.gov.uk/guidance/siren-study

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
284460

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 284460

Study information

Scientific Title

Sarscov2 Immunity & REinfection EvaluatioN: Impact of detectable anti-SARS-COV2 on the subsequent incidence of COVID-19 in healthcare workers

Acronym
SIREN

Study objectives
Prior COVID-19 infection with the subsequent detection of SARS-CoV-2 is protective against future clinical and asymptomatic infection

Primary objective:
To determine whether the presence of antibody to SARS-CoV-2 (anti-SARS-CoV-2) is associated with a reduction in the subsequent risk of re-infection over short term periods (reviewed monthly) and the next year.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/05/2020, South Central - Berkshire Research Ethics Committee (East Hampstead Baptist Church, South Hill Road, Bracknell, RG12 7NS, United Kingdom; +44 (0)2071048224; berkshire.rec@hra.nhs.uk), ref: 20/SC/0230

Study design
Prospective observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a copy of the participant information sheet

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Upon enrolment, participants will complete an online questionnaire and provide a blood sample for antibody testing and swabs for viral testing. Thereafter, every two to four weeks participants will be asked to provide further swab samples and complete a follow-up questionnaire to provide information on possible COVID-19 symptoms, exposures and enrolment in vaccine or treatment trials. On a monthly basis, participants will also be asked to provide further blood

samples for serological testing.. Participants will be followed up for 12 months from their enrolment.

The samples will be tested in local Trust labs but will also be used for central confirmatory antibody testing and serological characterisation, or for viral genome sequencing and/or culture.

Intervention Type
Other

Primary outcome measure
1. SARS-CoV-2 antibody measured in NHS laboratories using local assays (Roche Cobas or Abbott Platforms) measured monthly
2. SARS-CoV-2 infection measured using PCR test using local assays measured every two weeks

Secondary outcome measures
1. Symptoms of SARS-Cov-2 infection measured by a 2 weekly survey of participants developed and validated by study team including the 12 most commonly reported symptoms
2. Ability to culture viable virus from SARS-CoV-2 residual viral samples that are PCR positive submitted to PHE throughout the study, cultured in category 3 laboratory on vero cells
3. Identification of reinfection or persistent infection if second positive test after 90 days measured using SARS-CoV-2 viral RNA submitted to COG-UK sequencing laboratories for each positive PCR result
4. Serological response measured using SARS-CoV-2 residual positive sera submitted to PHE and measured using laboratory assays monthly
5. Serological response measured using enzyme immunoassay detection of IgG measured using laboratory assays monthly
6. NHS Trust, age, sex, staff group, ethnicity and co-morbidities as recorded by the participant recorded at baseline using a novel questionnaire
7. Phylogenetic relatedness of SARS-CoV-2 whole genome sequences on positive PCR samples, linked to MRC CLIMB in a secure data infrastructure with other samples submitted from hospitals and community in the same time period

Overall study start date
19/05/2020

Completion date
31/03/2028

Eligibility

Key inclusion criteria
Hospital healthcare worker willing to consent for regular follow up for 12 months with swabs and blood samples

Participant type(s)
Health professional

Age group
Adult

Sex
Both

Target number of participants
Minimum 10,000 Maximum 100,000

Total final enrolment
35768

Key exclusion criteria
Unwilling to participate in regular follow up

Date of first enrolment
18/06/2020

Date of final enrolment
31/03/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Free Hospital
Royal Free London NHS Trust
Pond St
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
UK Health Security Agency

Sponsor details
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United Kingdom

E14 5EA
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elizabeth.coates@ukhsa.gov.uk

Sponsor type
Government

Website
https://www.gov.uk/government/news/10-000-people-now-signed-up-to-covid-19-immunity-study

ROR
https://ror.org/018h10037

Funder(s)

Funder type
Government

Funder Name
Department of Health and Social Care

Alternative Name(s)
Department of Health & Social Care, DH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/04/2022

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol (preprint)		18/12/2020	08/01/2021	No	No
Preprint results	efficacy of BNT162b2 mRNA vaccine in preprint	22/02/2021	16/03/2021	No	No
Results article	Protection from reinfection by previous infection or vaccination	16/02/2022	17/02/2022	Yes	No
Protocol article		28/06/2022	30/06/2022	Yes	No
Results article	results on incidence of, risk factors for, and impact of vaccines on primary SARS-CoV-2 infection during the second wave in England	20/07/2022	21/07/2022	Yes	No
Results article	Nest case-control study investigating antibody correlates of protection	08/09/2022	12/09/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article	COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection	08/05/2021	04/02/2025	Yes	No
Results article	Early Warning Surveillance for SARS-CoV-2 Omicron Variants	01/12/2022	04/02/2025	Yes	No
Results article	Effect of second booster vaccinations and prior infection against SARS-CoV-2	14/12/2023	04/02/2025	Yes	No
Results article	infection rates of antibody-positive compared with antibody-negative health-care workers	17/04/2021	04/02/2025	Yes	No
Other publications	Longitudinal prospective cohort sub-study protocol to capture influenza and respiratory syncytial virus alongside SARS-CoV-2 in UK healthcare workers winter 2022/23 and beyond	11/07/2024	12/02/2025	Yes	No
Other publications	Evaluating blood sampling strategies within the SIREN study	01/07/2025	02/07/2025	Yes	No