ISRCTN11946807 https://doi.org/10.1186/ISRCTN11946807

Characterisation of COVID-19 long-term immunity

Submission date	Recruitment status	[_] Prospectively registered
10/11/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/11/2020	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
06/11/2024	Infections and Infestations	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
In March 2019 a new coronavirus (SARS-CoV-2) was identified that causes the disease COVID-19. This has caused a global pandemic, with millions of people infected. Many scientists are now working to develop vaccines and treatments to help slow the spread of the virus. Early results from 2 vaccine trials were reported in July and these were very promising. It was clear however, that scientists still do not know what level of immune response provides protection against the virus.
Reducing the infection rate and finding vaccines and treatments all require a better understanding of how the immune system responds to a COVID-19 infection. This study aims to look in detail at the long-term immune response of people who have been infected and compare this to the symptoms they had during the infection. It will also compare long-term health outcomes in people who have and have not had COVID-19.

Who can participate?
People who are part of the Avon Longitudinal Study of Parents and Children (aka Children of the 90s), will be invited to take part if we know whether or not they are likely to have been infected by the virus. We have this information from:
• an answer they gave in earlier questionnaires about COVID-19 OR
• the result of a blood test they completed at home (serology test) for Children of the 90s OR
• information in their NHS medical records indicates they had COVID-19 (if they gave consent for us to look at this)

What does the study involve?
Participants will attend up to 4 visits over a 12-month period.
Each visit is a 55-minute session at our centre in Oakfield House, where they will;
1. Provide a blood sample (5 tubes)
We will ask for a sample of blood, this will be taken in the usual way. Although we will need to collect 4 blood tubes from you this will not be more than 50ml of blood which is about a quarter of a teacup.
2. Provide a urine and saliva sample.
3. Complete the following physical measures:
Height and weight – We will measure height and weight so that we can work out current BMI

(Body Mass Index)
Respiratory function test – a simple sit to stand test to assess how well participants breath during exercise. They will be asked to get up from a chair and then sit back down as many times as they can in one minute. During this test they will wear a monitor to measure oxygen level and heart rate.
If a sit to stand test cannot be completed, then a 6-minute walk test will be completed instead.
4. Computer based questionnaire.
Participants will be asked to complete a short computer-based questionnaire about their quality of life.

What are the possible benefits and risks of participating?
There are no direct health benefits for taking part, and this is not a health check or a diagnostic test for COVID-19. We are asking participants to help us with research that could help with future treatment and vaccine development for COVID-19. There are no serious risks involved in taking part. Participants might find giving a blood sample slightly uncomfortable and might have a temporary bruise on their arm.

Where is the study run from?
This research is organised by Children of the 90s, University of Bristol, the principle investigator is Professor Nicholas Timpson. This study is part of the a larger study called 'A UK underpinning platform to study immunology and immunopathology of COVID-19:The UK Coronavirus Immunology Consortium' (or UK CIC), and the PI is Professor Paul Moss who is based at the University of Birmingham.

When is the study starting and how long is it expected to run for?
August 2020 to November 2021

Who is funding the study?
The study is funded by The Medical Research Council (UK)

Who is the main contact?
Ms Lynn Molloy (public), Lynn.Molloy@bristol.ac.uk
Prof Nicholas Timpson (scientific, PI), n.j.timpson@bristol.ac.uk

Contact information

Type(s)
Public

Contact name
Ms Lynn Molloy

Contact details
Chief Operating Officer
ALSPAC (Children of the 90s)
Population Health Sciences
Bristol Medical School
University of Bristol
Oakfield House
Oakfield Grove
Bristol

United Kingdom
BS8 2BN
+44 (0)117 455 9186
Lynn.Molloy@bristol.ac.uk

Type(s)
Scientific, Principal Investigator

Contact name
Prof Nicholas Timpson

ORCID ID
http://orcid.org/0000-0002-7141-9189

Contact details
University of Bristol - ALSPAC
Oakfield House
Oakfield Grove
Bristol
United Kingdom
BS8 2BN
+44 (0)117 455 0977
n.j.timpson@bristol.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
289646

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 47414, IRAS 289646

Study information

Scientific Title
Longitudinal study of physiological and immunological responses to COVID-19/SARS-CoV-2 infection in a population based study – Children of the 90s

Study objectives
There are long-term and detectable effects of SARS-CoV-2 infection after disease

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/10/2020, NHS HRA REC (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)20 7972 2545; hra.approval@nhs.net), ref: 20/HRA/4854

Study design
Observational; Design type: Cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Community

Study type(s)
Screening

Participant information sheet
http://www.bristol.ac.uk/media-library/sites/alspac/documents/participants/UKCIC_Participant_Information_Sheet.pdf

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

Interventions
ALSPAC will complete a case selection process to identify participants who are likely to have had a SARS-CoV-2 infection and controls who are unlikely to have had COVID-19. This will involve review of the following information already held by the ALSPAC study:
1. Participants with a positive antibody response as part of serological testing completed by cohort members
2. Review of linked NHS data, where participants have previously consented to linkage
3. Self report of a positive COVID-19 test or GP diagnosis via response to previous questionnaires, or self report of no symptoms or tests.

All those identified through the case selection (approx. 150 cases and up to 200 controls) will receive an initial invite email. Study information is provided via a link to the Participant Information Sheet. Participants will be asked to respond by phone or email if they wish to take part. They will then be called to book an initial 45 min appointment at the ALSPAC centre, Oakfield House, Bristol. A confirmation letter and link to visit information sheet will be sent. The day before the visit a reminder call will be made and this will include a check for any COVID-19 symptoms. If participants do not respond to the initial invite within 1 week a reminder message will be sent and after a further week on non-response a phone-call reminder.

At the visit the participant will be asked to complete the following procedures:
Informed consent - A 1-1 session with an ALSPAC Fieldworker
Blood sampling (4x10ml EDTA, 1x5ml Serum)
Saliva sample
Physical Measures - Height, weight
Respiratory function testing - A 1 minute sit to stand test or 6 minute walking test whilst having

oxygen saturation levels
and heart rate measured using sensor placed on the finger
Urine sample
Questionnaire - Computer based questionnaire asking about quality of life post infection and breathlessness

Following this initial visit blood and saliva samples will be tested for current immune response levels. Those with a seropositive result (approx. 50 participants) and controls with a Seronegative result (approx. 10) will be invited back for repeat visits (same as the first visit) at 3months, 6 months and 9-12 months after visit 1. Those who are not required to continue will be notified by email. Those eligible to continue will be sent an email message and will then be called to book an appointment. The same confirmation letter and appointment reminder letter will be sent.

Participants who notify us at any time of COVID-19 symptoms or positive COVID-19 test will be ineligible to continue
with the study.

Intervention Type
Other

Primary outcome measure
1. Presence in saliva of SARS-CoV-2 determined using reverse transcriptase polymerase chain reaction (RT-PCR assay) at baseline, 4 months and 9 months
2. Titres (concentration) of each antibody isotype (e.g. IgM, IgA, IgG) in blood samples specific to SARS-CoV-2 viral proteins/epitopes being produced determined by ELISA and Western blots. At baseline, 4 months and 9 months
3. B and T-cell immune response and characteristics of innate immune cell function by laboratory analysis of blood samples (flow cytometry, ELISpots, ELISA) at baseline, 4 months and 9 months
4. Immune response to COVID-19 and cross-reactive immune responses against other pathogens such as the circulating human CoVs by laboratory analysis of blood samples (B-cell receptor (BCR) sequencing, T-cell receptor (TCR) sequencing, NanoString analysis, RNAseq, single cell analysis, transciptomics, proteomics, cell signalling analysis, analysis of cellular cytotoxicity) at baseline, 4 months and 9 months
5. T-Cell, B-cell and antibody cross-reactivity and definition of how cross-reactivity may influence response to infection and/or vaccination by laboratory analysis of blood samples (B-cell receptor (BCR) sequencing, T-cell receptor (TCR) sequencing, NanoString analysis, RNAseq, single cell analysis, transciptomics, proteomics, cell signalling analysis, analysis of cellular cytotoxicity) at baseline, 4 months and 9 months

Secondary outcome measures
1. Exercise capacity by the completion of sit to stand or 6 min walk tests and measurement of heart rate and oxygen saturation at baseline, 4 months and 9 months
2. Quality of life by the completion of the SF36 questionnaire at baseline, 4 months and 9 months
3. BMI by measurement of height and weight at baseline, 4 months and 9 months

Overall study start date
01/08/2020

Completion date
30/11/2021

Eligibility

Key inclusion criteria
Participants of the ALSPAC cohort meeting the following criteria:
1. Aged 25 or over
2. Undergone SARS-CoV-2 antibody testing through the ALSPAC SARS-CoV-2 serology study (IRAS 289493)
3. Individuals who, through self-report or through linkage to official health records, are identified as being highly likely to have had COVID-19 infection (from either positive SARS-CoV-2 PCR test performed at NHS care facility, COVID-19 testing site or home testing)
4. Individuals who have been told by a physician that, in the opinion of that doctor, they have had a clinical illness likely to be COVID-19

Control participants
5. Aged 25 or over
6. Individuals who self-report as not experiencing symptoms of COVID-19 via the symptom survey
7. Self-report as not having had positive SARS-CoV-2 molecular test
8. Are confirmed SARS-CoV-2 seronegative at Visit 1

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 250; UK Sample Size: 250

Total final enrolment
372

Key exclusion criteria
Exclusion criteria for both controls and cases:
1. Do not wish to participate in this research study
2. Participants taking blood thinners or blood-thinning agents (e.g. warfarin) or with a known clotting disorder or other reason unable to provide a blood sample
3. Not willing to provide blood samples
4. Do not meet eligibility criteria for respective arm

Date of first enrolment
13/11/2020

Date of final enrolment
31/07/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Bristol
Oakfield House
Oakfield Grove
Bristol
United Kingdom
BS8 2BN

Sponsor information

Organisation
University of Bristol

Sponsor details
1 Cathedral Square
Bristol
England
United Kingdom
BS1 5DD
+44 (0)117 3940177
research-governance@bristol.ac.uk

Sponsor type
University/education

Website
http://bristol.ac.uk/

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Research council

Funder Name

Medical Research Council; Grant Codes: MR/V028448/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 13/05/2024:
We plan to publish two papers on the results of the sample collection and analysis both during the running of the year-long experiment (following analysis in cross-section), and also to analyse the collective product of the work (including longitudinal analysis) at the end of the planned experiment time. These results fall as part of the UK Coronavirus Immunology Consortium (https://www.uk-cic.org) which has an established engagement and communications plan and also within the National Core Studies for Longitudinal Health and Wealth – which will be reporting results both in published papers and through HDRUK to UK SAGE.

The protocol is available on request.

Previous publication and dissemination plan:
We plan to publish the results of the sample collection and analysis both during the running of the year-long experiment (following analysis in cross-section), and also to analyse the collective product of the work (including longitudinal analysis) at the end of the planned experiment time. These results fall as part of the UK Coronavirus Immunology Consortium (https://www.uk-cic.org) which has an established engagement and communications plan and also within the National Core Studies for Longitudinal Health and Wealth – which will be reporting results both in published papers and through HDRUK to UK SAGE.

The protocol is available on request.

Intention to publish date
01/06/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. Data will form part of the ALSPAC repository and will be shared according to the access policy http://www.bristol.ac.uk/alspac/researchers/access/

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.0	02/02/2021	12/08/2022	No	No
HRA research summary			28/06/2023	No	No