

# What's the STORY: serum testing of representative youngsters including SARS-CoV-2 (COVID-19), diphtheria and meningitis C

<b>Submission date</b>	<b>Recruitment status</b>	<input type="checkbox"/> Prospectively registered
25/07/2019	No longer recruiting	<input checked="" type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
01/06/2020	Completed	<input checked="" type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
12/09/2023	Infections and Infestations	

## Plain English summary of protocol

### Background and study aims

The aim of this study is to help understand the story of infectious diseases in England. One of the ways bodies develop protection against infectious diseases is by developing antibodies, either after an infection or following vaccination. Researchers can measure the antibodies to see how well-protected people are from those infectious diseases. To start with they are looking at COVID-19, group C meningococcus (MenC) and diphtheria. By looking for antibodies against infectious diseases such as COVID-19 they can tell what proportion of the population has come into contact with the disease.

### Who can participate?

Group 1: Male or female, aged 0 - 24 inclusive

Group 2: Male or female, aged 0 - 19 inclusive

Group 3: Male or female, aged 0 - 19 from the BAME population

### What does the study involve?

The researchers are working with Public Health England to collect blood and saliva samples from a selection of 0-24-year-olds from across England. Basic demographic characteristics will be collected by questionnaire and/or case report form and will include: date of birth, gender, GP details, ethnic group, association with communities of special interest, household income and vaccination history.

### What are the possible benefits and risks of participating?

This information collected will help Public Health England and the Scientific Advisory Group for Emergencies (SAGE) make decisions on how they manage the COVID-19 pandemic response now and in the future.

### Where is the study run from?

University of Oxford (UK)

When is the study starting and how long is it expected to run for?  
July 2019 to June 2022

Who is funding the study?  
National Institute for Health Research (NIHR) (UK)

Who is the main contact?  
Dr Helen Ratcliffe  
whatsthestory@ovg.ox.ac.uk

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Helen Ratcliffe

**Contact details**  
Oxford Vaccine Group Churchill Hospital,  
Old Road, Headington  
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OX3 7LE  
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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**Integrated Research Application System (IRAS)**  
263097

**ClinicalTrials.gov (NCT)**  
NCT04061382

**Protocol serial number**  
CPMS 42523, IRAS 263097

## Study information

**Scientific Title**  
Sero-epidemiological survey of England in 2019/2020

**Acronym**  
What's the STORY

## Study objectives

Current hypothesis as of 18/12/2020:

Public Health England has an ongoing sero-prevalence programme to assess how well the population is protected from vaccine preventable diseases. The current way to check this is by testing left over blood samples from participating healthcare laboratories around the country. However, these samples may not be representative of the general population, particularly in younger age groups who are often most at risk from vaccine preventable diseases. In the Netherlands, they use a different system to assess how well the population is protected from vaccine preventable diseases, actively collecting blood samples from a representative cross section of society. This type of approach would address the limitations of using residual serum samples and allows the collection of additional relevant history e.g. number of family members and previous vaccines received. The investigators are therefore proposing a pilot study to assess the feasibility of establishing a national sero- epidemiological survey in England in individuals aged 0 - 24 years. The investigators will be focusing initially on diphtheria and group C invasive meningococcal disease, both of which are vaccine preventable. This will involve enrolling 2300 participants in the study from different geographical and socioeconomic backgrounds across our test sites and taking a blood sample. This blood will be analysed to look at the level of immunity to vaccine preventable diseases.

The original protocol has been amended to include the testing of antibodies against other infectious diseases, specifically COVID-19. A second group has been added to recruit an additional 500 to 1200 participants between the ages of 0-19 years. The additional funding has been used to open two more sites to recruit to group two across regions in England that are currently not represented by this study. Having a large number of blood samples from a range of age groups is useful when gathering information about an emerging disease such as the current novel coronavirus (COVID-19). These samples can help provide answers regarding the true number of infections with SARS-CoV-2 (the virus which causes COVID-19 disease) in this population. Group 2 can be enhanced by the samples received from other ethically approved research projects where participants have consented for their samples being used outside of the study.

Additional funding has been granted for the addition of 300 participants from the BAME community, who will form Group 3. Data from Group 3 would be invaluable in understanding whether higher rates of disease in the BAME community are a result of greater exposure to COVID-19 contact, a higher likelihood of being infected once exposed or a greater risk of disease once infection occurs.

In addition to increasing the sample size and the number of regions in the UK that are being sampled, a longitudinal sampling cohort has been introduced. A subset of participants equally distributed over the age bands will be enrolled into the longitudinal aspect of the study where repeat blood and saliva samples are taken to look for antibodies against SARS-CoV-2. A questionnaire to ascertain whether the participant or any household contacts have had any symptoms of or been tested positive for COVID-19 will also be collected.

A proportion of participants from this group from selected sites will also provide up to a maximum of three blood samples for separation of peripheral blood mononuclear cells (PBMCs) to evaluate T cell responses. These participants can be either seronegative or seropositive at their Visit 1.

With the latter addition of four more sites, all NHS regions are now represented in the study.

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Previous hypothesis:

Public Health England has an ongoing seroprevalence programme to assess how well the population is protected from vaccine-preventable diseases. The current way to check this is by testing leftover blood samples from participating healthcare laboratories around the country. However, these samples may not be representative of the general population, particularly in younger age groups who are often most at risk from vaccine-preventable diseases. In the Netherlands, they use a different system to assess how well the population is protected from vaccine-preventable diseases, actively collecting blood samples from a representative cross-section of society. This type of approach would address the limitations of using residual serum samples and allows the collection of additional relevant history e.g. number of family members and previous vaccines received. The investigators are therefore proposing a pilot study to assess the feasibility of establishing a national seroepidemiological survey in England in individuals aged 0 - 24 years. The investigators will be focusing initially on diphtheria and Group C invasive meningococcal disease, both of which are vaccine-preventable. This will involve enrolling 2300 participants in the study from different geographical and socioeconomic backgrounds across our test sites and taking a blood sample. This blood will be analysed to look at the level of immunity to vaccine-preventable diseases.

The original protocol has been amended to include the testing of antibodies against other infectious diseases, specifically COVID-19. A second group has been added to recruit an additional 500 to 1200 participants between the ages of 0-19 years. The additional funding has been used to open two more sites to recruit to group two across regions on England that are currently not represented by this study. Having a large number of blood samples from a range of age groups is useful when gathering information about an emerging disease such as the current novel coronavirus (COVID-19). These samples can help provide answers regarding the true number of infections with SARS-CoV-2 (the virus which causes COVID-19 disease) in this population.

In addition to increasing the sample size and the number of regions in the UK that are being sampled a longitudinal sampling cohort has been introduced. Approximately 20% of participants equally distributed over the age bands will be enrolled into the longitudinal aspect of the study where repeat blood and saliva samples are taken to look for antibodies against SARS-CoV-2. A questionnaire to ascertain whether the participant or any household contacts have had any symptoms of or been tested positive for COVID-19 will also be collected.

Added 29/07/2020:

A proportion of participants from this group from selected sites will also provide up to a maximum of three blood samples for separation of peripheral blood mononuclear cells (PBMCs) to evaluate T cell responses. These participants can be either seronegative or seropositive at their Visit 1.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 20/06/2019, London - Surrey Research Ethics Committee (Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 1048310; surrey.rec@hra.nhs.uk), REC ref: 19/LO/1040

### **Study design**

Prospective cross-sectional seroprevalence study

## **Primary study design**

Observational

## **Study type(s)**

Screening

## **Health condition(s) or problem(s) studied**

Diphtheria, group C meningococcus infection, COVID-19 (SARS-CoV-2 infection)

## **Interventions**

This is a pilot study to assess the feasibility of establishing a national seroepidemiological survey in England in individuals aged 0-24 years, focusing initially on diphtheria and group C invasive meningococcal disease. The researchers are aiming to recruit 2300 individuals and are aiming to ensure that sample is broadly representative of the region according to IMD (Index of Multiple Deprivation scores). The PHE generated a list of all postcodes in recruiting regions and determining the quintiles of IMD within that region. Participants interested in taking part in the study will contact sites to arrange a visit. Basic demographic characteristics will be collected by questionnaire and/ or case report form (CRF) and will include: DOB, gender, GP details, ethnic group, association with communities of special interest, household income and vaccination history.

### **Randomised selection of population - Group 1**

Group 1 will be focusing on COVID-19, diphtheria and group C invasive meningococcal disease. The investigators are aiming to recruit around 2300 individuals and the investigators are aiming to ensure that sample is broadly representative of the region according to IMD (Index of Multiple Deprivation scores). PHE has generated a list of all postcodes in recruiting regions and determining the quintiles of IMD within that region. Participants interested in taking part in the study will contact sites to arrange a visit. Basic demographic characteristics will be collected by questionnaire and/ or case report form (CRF) and will include: DOB, gender, GP details, ethnic group, association with communities of special interest, household income and vaccination history.

### **Group 2**

Group 2 will focus on 0-19-year-olds only. They will not be restricted to postcode sampling. Instead, this will include standard recruitment methods such as social media advertisements within the normal recruiting regions for each site.

Added 29/07/2020:

A proportion of participants from this group from selected sites will also provide up to a maximum of three blood samples for separation of peripheral blood mononuclear cells (PBMCs) to evaluate T cell responses. These participants can be either seronegative or seropositive at their Visit 1.

Added 18/12/2020:

### **Group 3**

Group three will consist of up to 300 participants aged 0-19 from the Black, Asian and Minority ethnic population aged 0-19 years. They will not be restricted to the post code sampling and will be recruited at a sub-set of sites depending on capacity and the demographic profile of the local population. Recruitment will be by multiple approaches, including mail outs and advertising in

community (e.g. community centres, religious establishments) or GP practices where we have ethics approval for them to act as PICs. These can vary according to each site's experience and their contacts within their local community on how is best to approach the BAME community.

## **Intervention Type**

Other

## **Primary outcome(s)**

1. Feasibility of a population-based seroepidemiological programme measured by response rate and participation in the study as proved by questionnaire completion, sample collection and database records at baseline
2. Added public health benefit measured by comparison with serological markers of immunity for vaccine-preventable diseases as measured in an age-matched cohort in the current residual sera programme which will occur at the end of the study

## **Key secondary outcome(s)**

Current secondary outcome measures as of 18/12/2020:

1. Effectiveness of recruitment methods measured by the number and rate of successfully enrolled participants at Visit 1
2. Antibody concentrations against infections and vaccine-preventable diseases starting with diphtheria, menC and SARS-CoV-2; measures include Anti-Diphtheria Toxoid concentrations, serum bactericidal activity (SBA) titres and serum IgG to SARS-CoV-2 antigens, including spike protein and/or nucleocapsid (as measured by ELISA and/or neutralising assay). SARS COV-2 samples will be tested as samples are being collected whereas serum for diphtheria and menC will be tested at the end of the study
3. Prevalence, kinetics of antibodies, of SARS-CoV-2 infections in 0–19-year-olds, and variation in prevalence in time, age and geography, measured by ELISA and/or neutralising assay at baseline and 3 subsequent visits every 2-3 months
4. Serum and salivary antibodies against SARS-CoV-2 measured by ELISA in 3 visits every 2-3 months following baseline

Exploratory outcome measures:

1. Presence of SARS-CoV-2 virus in saliva measured by saliva swab in 3 visits every 2-3 months following baseline
2. Recruitment strategies between groups measured with demographic data collected by the questionnaire and regional census data at baseline
3. T cell responses to SARS-CoV-2 antigens including, but not limited to S, M and N proteins, as measured by techniques including, but not limited to ELISpot ICS Proliferation assay at the 3 subsequent visits
4. Antigen-specific IgG and T cells against non-SARS-CoV-2 coronaviruses (e.g. NL62 and 229E) at the 3 subsequent visits every 2-4 months

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Previous secondary outcome measures:

1. Effectiveness of recruitment methods measured by the number and rate of successfully enrolled participants at Visit 1
2. Antibody concentrations against infections and vaccine-preventable diseases starting with diphtheria, menC and SARS-CoV-2; measures include Anti-Diphtheria Toxoid concentrations,

serum bactericidal activity (SBA) titres and serum IgG to SARS-CoV-2 antigens. SARS COV-2 samples will be tested as samples are being collected whereas serum for diphtheria and menC will be tested at the end of the study

3. Prevalence, kinetics of antibodies, of SARS-CoV-2 infections in 0-19-year-olds, and variation in prevalence in time, age and geography, measured by ELISA and/or neutralising assay at baseline and 3 subsequent visits every 2-3 months

4. Serum and salivary antibodies against SARS-CoV-2 measured by ELISA in 3 visits every 2-3 months following baseline

Exploratory outcome measures:

1. Presence of SARS-CoV-2 virus in saliva measured by saliva swab in 3 visits every 2-3 months following baseline

2. Recruitment strategies in Group 1 and Group 2 measured with demographic data collected by the questionnaire and regional census data at baseline

Added 29/07/2020:

3. T cell responses to SARS-CoV-2 antigens including, but not limited to S, M and N proteins, as measured by techniques including, but not limited to ELISpot ICS Proliferation assay at the 3 subsequent visits every 2-4 months

4. Antigen-specific IgG and T cells against non-SARS-CoV-2 coronaviruses (e.g. NL62 and 229E) at the 3 subsequent visits every 2-4 months

## Completion date

30/06/2022

## Eligibility

### Key inclusion criteria

Current inclusion criteria as of 18/12/2020:

1. Parents/legal guardians or adult participant is willing and able to give informed consent for participation in the study

2. Male or Female, aged 0 - 24 years inclusive (Group 1) and 0 - 19 inclusive (Group 2 and 3)

3. Parents/legal guardians or adult participants are willing to allow their General Practitioner or relevant NHS databases to be contacted for a full immunisation history

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Previous inclusion criteria:

1. Parents/legal guardians or adult participant\* is willing and able to give informed consent for participation in the study.

2. Male or female, aged 0 - 24 years inclusive (Group 1)

3. Male or female, aged 0 - 19 years inclusive (Group 2)

4. Parents/legal guardians or adult participants are willing to allow their General Practitioner or relevant NHS databases to be contacted for a full immunisation history

### Participant type(s)

Healthy volunteer

### Healthy volunteers allowed

No

**Age group**

Mixed

**Sex**

All

**Total final enrolment**

3600

**Key exclusion criteria**

Current exclusion criteria as of 18/12/2020:

1. Group 1 only If participants do not live in the postcode districts selected by PHE (Group 1 only)
2. Group 3 only if participants are not from the BAME population
3. Participants who have a member of their household already enrolled in the study where their ages are less than 5 years apart
4. Any significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the research study, or may influence the result of the research study, or the participant's ability to participate in the research study. Examples of disorders or diseases which would be excluded include:
  - 4.1. Medically diagnosed bleeding disorder
  - 4.2. Medically diagnosed platelet disorder
  - 4.3. Anticoagulant medication
  - 4.4. Pregnancy

Temporary exclusion criteria:

The participant may not enter the study if they or any member of their household is under temporary isolation measures for suspected SARS-CoV-2 infection

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Previous exclusion criteria:

If participants do not live in the postcode districts selected by PHE (Group 1 only)

1. Medically diagnosed bleeding disorder
2. Medically diagnosed platelet disorder
3. Anticoagulation medication
4. Pregnancy
5. If another member of their household is participating who is within 5 years of age of the potential participant's age

Temporary exclusion criteria:

The participant may not enter the study if they or any member of their household is under temporary isolation measures for suspected SARS-CoV-2 infection.

**Date of first enrolment**

15/10/2019

**Date of final enrolment**

30/06/2021

## Locations

### Countries of recruitment

United Kingdom

England

### Study participating centre

#### University of Oxford

Oxford Vaccine Group

Churchill Hospital

Old Road

Headington

Oxford

United Kingdom

OX3 7LE

### Study participating centre

#### Bradford Teaching Hospitals NHS Foundation Trust

NIHR Clinical Research Network: Yorkshire and Humber

Neonatal Research Office, Transitional care, M2

Bradford

United Kingdom

BD9 6RJ

### Study participating centre

#### University Hospitals Bristol NHS Foundation Trust

Level 6, UH Bristol Education and Research Centre

Upper Maudlin Street

Bristol

United Kingdom

BS2 8AE

### Study participating centre

#### Leeds Teaching Hospitals NHS Trust

Great George Street

Leeds

United Kingdom

LS1 3EX

**Study participating centre**

**Royal Manchester Children's Hospital**  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**Sheffield Children's Hospital**  
Research and Innovation  
D Floor Stephenson Wing  
Sheffield Children's Hospital  
Western Bank  
Sheffield  
United Kingdom  
S10 2TH

**Study participating centre**

**University Hospital Southampton NHS Foundation Trust**  
SGH – Level E, Laboratory & Pathology Block, LE123 – MP 138  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**

**St George's University Hospitals NHS Foundation Trust**  
Paediatric Infectious Diseases Research Group  
St. Georges University of London  
Jenner Wing, Level 2, Room 2.216F, Mail Point J2C  
London  
United Kingdom  
SW17 0RE

**Study participating centre**

**University of Nottingham Health Service**  
Cripps Health Centre  
University Park  
Nottingham  
United Kingdom  
NG7 2QW

**Study participating centre**

**University Hospitals Plymouth NHS Trust**  
Derriford Road  
Crownhill  
Plymouth  
United Kingdom  
PL6 8DH

**Study participating centre**

**Freeman Hospital**  
Newcastle Upon Tyne Hospital Trust  
Freeman Road  
High Heaton  
Newcastle  
United Kingdom  
NE7 7DN

**Study participating centre**

**St. Mary's Hospital**  
Imperial College Healthcare NHS Trust  
Praed Street  
London  
United Kingdom  
W2 1NY

**Study participating centre**

**West Suffolk NHS Foundation Trust**  
Hardwick Lane  
Bury St Edmunds  
United Kingdom  
IP33 2QZ

**Study participating centre**

**Heartlands Hospital**  
University Hospitals Birmingham NHS Foundation Trust  
Bordesley Green East  
Birmingham  
United Kingdom  
B9 5SS

## **Sponsor information**

**Organisation**

University of Oxford

**ROR**

<https://ror.org/052gg0110>

**Funder(s)****Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study will be available upon request from Helen Ratcliffe, [helen.ratcliffe@paediatrics.ox.ac.uk](mailto:helen.ratcliffe@paediatrics.ox.ac.uk). The type of data are: ID of the site, gender, age, IMD, ethnicity, date of sample collection, assay results, date of subsequent visit with the type of sample and assays, symptomatology of participant and household, education attendance at the time of sampling. The study protocol, statistical analysis plan and analytic code will also be available. The data will be available from 3 months to 5 years following article publication to researchers who provide a methodologically sound proposal. To gain access, data requestors will need to sign a data access agreement.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		20/07/2022	23/03/2023	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version v7.0	21/07/2020	01/12/2020	No	No
<a href="#">Protocol file</a>	version 9.0	28/06/2021	09/07/2021	No	No
<a href="#">Protocol file</a>	version 9.1	20/08/2021	27/08/2021	No	No
<a href="#">Protocol file</a>	version 9.2	25/10/2021	05/11/2021	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes