ISRCTN11952463 https://doi.org/10.1186/ISRCTN11952463

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

Submission date
25/07/2019

Recruitment status
No longer recruiting

Registration date
01/06/2020

Overall study status
Completed

Last Edited
12/09/2023

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
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

Study website
http://whatsthestory.org.uk

Contact information

Type(s)
Scientific

Contact name
Dr Helen Ratcliffe

Contact details
Oxford Vaccine Group Churchill Hospital,
Old Road, Headington
Oxford
United Kingdom
OX3 7LE
+44 (0)1865 611400
whatsthestory@ovg.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
263097

ClinicalTrials.gov number
NCT04061382

Secondary identifying numbers
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 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. 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.

———

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

Secondary study design
Cross sectional study

Study setting(s)
Community

Study type(s)
Screening

Participant information sheet
Participant information sheets are available on the website http://whatsthestory.org.uk under each study site location

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 measure
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

Secondary outcome measures
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

_____

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

Overall study start date
04/07/2019

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

———

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

Age group
Mixed

Sex
Both

Target number of participants
Up to 3,800

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

———

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
England

United Kingdom

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

Sponsor details
Joint Research Office
1st Floor, Boundary Brook House
Churchill Hospital
Old Road, Headington
Oxford
England
United Kingdom
OX3 7LE
+44 (0)1865 611400
info@ovg.ox.ac.uk

Sponsor type
University/education

Website
https://www.ovg.ox.ac.uk/

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

Publication and dissemination plan
The study protocol is available on http://whatsthestory.org.uk.

The investigators will coordinate the dissemination of data from this study. All publications (e.g. manuscripts, abstracts, oral/slide presentations, book chapters) based on this study will be reviewed by all investigators prior to submission. Participants will have access to a summary of our study results either by post or an emailed link to our website with an abstract.

Intention to publish date
30/06/2022

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. 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?
Protocol file	version v7.0	21/07/2020	01/12/2020	No	No

Protocol file	version 9.0	28/06/2021	09/07/2021	No	No
Protocol file	version 9.1	20/08/2021	27/08/2021	No	No
Protocol file	version 9.2	25/10/2021	05/11/2021	No	No
Results article		20/07/2022	23/03/2023	Yes	No
HRA research summary			28/06/2023	No	No