ISRCTN12821688 https://doi.org/10.1186/ISRCTN12821688

Observational cohort trial of immune response in patients with chronic health conditions following coronavirus vaccination

Submission date
15/02/2021

Recruitment status
No longer recruiting

Registration date
17/02/2021

Overall study status
Completed

Last Edited
30/06/2025

Condition category
Cancer

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

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-to-see-how-the-covid-19-vaccination-affects-how-the-body-fights-infection-octave

Background and study aims
The rapid development and subsequent authorisation of vaccines against coronavirus (formal name SARS-CoV-2) has been a major step forward for medical science. The participants of developmental vaccine trials were generally healthy volunteers and questions remain as to the level of protection these vaccines will afford patients with chronic illnesses who may have deficiencies in their immune system and may not generate the same protective responses observed in healthy volunteers.
In summer 2021 COVID-19 vaccines started to be offered to young immune-suppressed people, aged 12 to 17 years. The rollout of COVID-19 vaccines to immune suppressed 5 to11-year-old children began in February 2022 in all four nations. To help work out optimal vaccine schedules, the OCTAVE trial has been expanded to include these younger participants. These participants were excluded from the existing studies of SARS-CoV-2 vaccines in those aged between 5 and 17 years and 364 days.
The aim is to evaluate the way the body defends itself against coronavirus (the immune response) following vaccination in clinically vulnerable groups.

Who can participate?
Adult groups (18 years or above): patients with end-stage kidney disease, liver disease or gastrointestinal disease on immune suppressive therapy, cancer, immune-mediated rheumatic diseases (e.g. rheumatoid arthritis) and stem cell transplant recipients who are receiving the COVID-19 vaccine as part of the national vaccination programme.
Children and adolescents group (aged 5 to 17 years): patients who are immune-suppressed due to medication following solid organ transplantation, with immune-mediated rheumatic diseases, or due to treatment for cancer or cancer itself who are receiving the COVID-19 vaccine as part of the national vaccination programme. Trial entry may precede either first, second, third or fourth vaccine dose.

What does the study involve?
Blood and saliva samples will be collected at the following time points:
Deep immunophenotyping Group:
• Before the first injection (unless the participant has already donated a blood sample as part of another study and these are available for use in OCTAVE)
• The day after the first injection (this is optional)
• Before the boost injection
• 28 days after the boost injection
• 6 months after the second injection
• 12 months after the first injection
Serology Group:
• Before the first injection (where this is possible)
• 28 days after the boost injection
Serology Plus Group:
• Before the injection of vaccine being given at trial entry. This may be the first, second, third or fourth injection of the vaccine depending on how many doses of vaccine they have received before entering the study.
• 28 days after the injection (-7/+56 days)
• If the participant has another injection of vaccine during the study, 28 days after this injection (-7/+56 days)
• 6 months after the most recent injection

What are the possible benefits and risks of participating?
There may be no direct benefit to the participants from taking part in this study. The information gained from this study may help to improve the way in which patients with chronic health conditions and cancer are vaccinated for coronavirus in the future.
Participants may need to go to hospital more frequently to have blood samples taken. How many extra visits are needed will depend on the patient's condition and how frequently they are currently being seen by their doctor. Where possible the study doctor and research nurse will try to limit the number of extra visits needed.
Having blood taken may cause some discomfort, bleeding or bruising where the needle enters the body and, in rare cases, light-headedness and fainting.

Where is the study run from?
The study is being run by the Cancer Research UK Clinical Trials Unit at the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2021 to June 2025

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

Who is the main contact?
OCTAVE Trial Office
OCTAVE@trials.bham.ac.uk

Study website
https://www.birmingham.ac.uk/octave

Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2021-000569-33

IRAS number
294480

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MX1034, sponsor number RG_21-007, IRAS 294480

Study information

Scientific Title
Observational Cohort Trial-T-cells Antibodies and Vaccine Efficacy in SARS-CoV-2

Acronym
OCTAVE

Study objectives
Current study hypothesis as of 02/08/2022:
The rapid development and subsequent authorisation of vaccines against coronavirus (formal name SARS-CoV-2) has been a major step forward for medical science. The participants of developmental vaccine trials were generally healthy volunteers and questions remain as to the level of protection these vaccines will afford patients with chronic illnesses who may have deficiencies in their immune system and may not generate the same protective responses observed in healthy volunteers.

In summer 2021 COVID-19 vaccines started to be offered to young immune-suppressed people, aged 12 to 17 years. The rollout of COVID-19 vaccines to immune-suppressed 5 to 11-year-old children began in February 2022 in all four nations. To help work out optimal vaccine schedules, the OCTAVE trial has been expanded to include these younger participants. These participants were excluded from the existing studies of SARS-CoV-2 vaccines in those aged between 5 and 17 years and 364 days.

The aim is to evaluate the way the body defends itself against coronavirus (the immune response) following vaccination in clinically vulnerable groups.

Previous study hypothesis:
The rapid development and subsequent authorisation of vaccines against coronavirus (COVID-19) has been a major step forward for medical science. In the UK, three vaccines are already approved by the regulatory agency, Pfizer/BioNTech, AstraZeneca, and Moderna. It is likely that further vaccines will become available in the coming months. National vaccination programmes have been initiated in the UK for Pfizer-BioNtech and the Astra-Zeneca vaccines. The populations evaluated in the trials of these vaccines were generally healthy volunteers. Therefore questions remain as to the level of protection these vaccines will afford patient populations with chronic healthcare conditions who may have immune deficiencies and, therefore, may not generate the same protective responses observed in healthy volunteers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/02/2021, London-Chelsea Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 1048029; chelsea.rec@hra.nhs.uk), ref: 21/HRA/0489

Study design
Multi-centre multi-disease prospective observational cohort trial

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Adult groups (18 years or above): patients with end-stage kidney disease, liver disease or gastrointestinal disease on immune suppressive therapy, cancer, immune-mediated rheumatic diseases (e.g. rheumatoid arthritis) and stem cell transplant recipients who are receiving the COVID-19 vaccine as part of the national vaccination programme. Children and adolescents group (aged between 5 and 17 years): patients who are immune-suppressed due to medication following solid organ (heart +/- lung, kidney) transplantation, with immune-mediated rheumatic diseases, or due to treatment for cancer or cancer itself who are receiving the COVID-19 vaccine as part of the national vaccination programme.

Interventions
Current interventions as of 08/08/2022:
Three different groups of research samples are being assessed during the trial:

Deep Immunophenotyping Group - each disease cohort will include 150 participants; blood and saliva samples are being collected at 4-5 time points;

Serology Group – each disease cohort will include up to 850 participants; blood and saliva samples are being collected twice;

Serology Plus Group – comprising three disease cohorts: paediatric cancer, post solid organ transplant and rheumatic/inflammatory conditions; cohorts to include up to 160 participants. Pre- and post-vaccine dose blood samples to be obtained (with a maximum of 4 sample timepoints per participant).

Blood and saliva samples will be collected at the following time points:

Deep immunophenotyping Group:
• Before the first injection (unless the participant has already donated a blood sample as part of another study and these are available for use in OCTAVE)
• The day after the first injection (this is optional)
• Before the boost injection
• 28 days after the boost injection
• 6 months after the second injection
• 12 months after the first injection

Serology Group:
• Before the first injection (where this is possible)
• 28 days after the boost injection

Serology Plus Group – Blood samples only:
• Before the injection of vaccine being given at trial entry. This may be the first, second, third or fourth injection of the vaccine depending on how many doses of vaccine they have received before entering the study.
• 28 days after the injection (-7/+56 days)
• If the participant has another injection of vaccine during the study, 28 days after this injection (-7/+56 days)
• 6 months after the most recent injection

Previous interventions as of 02/08/2022:
Three different groups of research samples are being assessed during the trial:

Deep Immunophenotyping Group - each disease cohort will include 150 participants; blood and saliva samples are being collected at 4-5 time points;

Serology Group – each disease cohort will include up to 850 participants; blood and saliva samples are being collected twice;

Serology Plus Group – comprising three disease cohorts: paediatric cancer, post solid organ transplant and rheumatic/inflammatory conditions; cohorts to include up to 160 participants. Pre- and post-vaccine dose blood samples to be obtained (with a maximum of 4 sample timepoints per participant).

Blood and saliva samples will be collected at the following time points:

Deep immunophenotyping Group:
• Before the first injection (unless the participant has already donated a blood sample as part of another study and these are available for use in OCTAVE)
• The day after the first injection (this is optional)
• Before the boost injection
• 28 days after the boost injection
• 6 months after the first injection

Serology Group:
• Before the first injection (where this is possible)
• 28 days after the boost injection

Serology Plus Group – Blood samples only:
• Before the injection of vaccine being given at trial entry. This may be the first, second, third or fourth injection of the vaccine depending on how many doses of vaccine they have received before entering the study.
• 28 days after the injection (-7/+56 days)
• If the participant has another injection of vaccine during the study, 28 days after this injection (-7/+56 days)

Previous interventions:
Two different groups of research samples are being assessed during the trial: Deep Immunophenotyping Group - each disease cohort will include 150 participants; and the Serology Group – each disease cohort will include up to 850 participants.

Blood and saliva samples are being collected at 4-5 time points for the Deep Immunophenotyping Group and twice for the Serology Group.

Blood and saliva samples will be collected at the following time points:

Deep immunophenotyping Group:
• Before the first injection (unless the participant has already donated a blood sample as part of another study and these are available for use in OCTAVE)
• The day after the first injection (this is optional)
• Before the boost injection
• 28 days after the boost injection
• 6 months after the first injection

Serology Group:
• Before the first injection (where this is possible)
• 28 days after the boost injection

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
Pfizer/BioNTech, AstraZeneca, and Moderna vaccines

Primary outcome measure
1. Anti-SARS-CoV-2 IgG Abs following vaccination will be measured using the Roche platforms. (The Roche assay measures the presence and amount of serum antibodies to both the spike (S) and the nucleocapsid (N) antigens of SARS-CoV-2. This assay will enable the discrimination of IgG responses to SARS-CoV-2 that results from vaccination and/or SARS-CoV-2 infection)
2. T cell responses to SARS-CoV-2 peptides following vaccination will be measured using the Oxford Immunotec modified T-SPOT Discovery SARS-CoV-2 assay. This IFNg ELISpot assay will provide insights into patient reactivity to SARS-CoV-2 S1, S2, Nucleocapsid and membrane peptides.

Secondary outcome measures
Measured following vaccination:

1. First symptomatic, PCR-proven COVID-19 occurrence from 14 days after first dose of SARS-CoV-2 vaccine in participants without evidence of prior infection with SARS-CoV-2 measured using PCR test
2. Humoral Immunogenicity: SARS-CoV-2 IgG (pseudo)neutralisation assays to assess the capacity of vaccine induced SARS-CoV-2 Abs to neutralise/block SARS-CoV-2 infection

Cellular Immunogenicity:
3. The relative contribution of T cell subsets and T cell function will be assessed using intracellular cytokine analysis and flow cytometry (ICCS) - established at Oxford University laboratories
4. Proliferation assays (CTV assay) will evaluate the recall potential of SARS-CoV-2 memory T cells at later (6 month) time points (established at Oxford University laboratories

Additional assays relevant to immune state and response may be undertaken:
5. Serum antibodies (IgG/IgM/IgA) to important SARS-CoV-2 antigens and SARS-CoV-2 related antigens (including but not limited to SARS, MERS and circulating seasonal coronaviruses: CoV-2 S, NL63 S, CoV-2 N, CoV-1 S, MERS S, HKU1 S, OC43 S, 229E S, CoV-2 RBD) will be measured in an MSD assay or bespoke ELISA established at University of Glasgow laboratories
6. Saliva antibodies (IgG/IgA) to both the spike (S) and the nucleocapsid (N) antigens of SARS-CoV-2 will be measured using an optimised saliva ELISA
7. Flow cytometric characterisation of the circulating immune compartment (e.g. T cells and B cells) will be undertaken
8. T cell and B cell specific responses to defined peptides/stimuli will be undertaken using established ELISpot assays, at Imperial College London and Oxford University laboratories

Overall study start date
04/01/2021

Completion date
30/06/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 02/08/2022:
1. Are eligible for vaccination by one of the SARS-CoV-2 vaccines approved by the MHRA administered in accordance with national guidelines and current versions of the applicable information for healthcare professionals (see Section 7.1) and:
1.1. For the Deep Immunotherapy Group only, have not received the second dose of the vaccine (booster)
1.2. For the Serology Group only, have not passed the 28 days (-7/+56 days) post second vaccine dose (booster)
1.3. For the Serology Plus Group, have not passed 28 days (within -7/+56 days) post second vaccine dose (booster) or up to 6 months post second vaccine dose, including patients who have received a third or further dose in that time period
2. Anticipated life expectancy of 6 months or greater
3. Fall into one (or more) of the following patient cohorts who will meet disease relevant classification, disease state, and staging according to established international standards:
3.1. Diagnosed with any of the following malignancies:
3.1.1. Breast
3.1.2. Lung
3.1.3. Acute Myeloid Leukaemia
3.1.4. Multiple Myeloma
3.1.5. Paediatric Cancer: any diagnosis of cancer in a child (aged 5 to < 18 years):
3.1.5.1. On active treatment
3.1.5.2. Within 6 months of completion of treatment
3.2. Diagnosed with the following rheumatic/inflammatory conditions:

3.2.1. Specialist diagnosis of relevant condition
3.2.2. Established on relevant therapy for ≥ 30 days
3.2.3. Meet the definitions in any of the following cohorts:
3.2.3.1. Deep Immunophenotyping Group::
3.2.3.1.1. Methotrexate plus inflammatory arthritis (to include RA, PsA, seronegative arthritis, and spondyloarthritis)
3.2.3.1.2. TNF inhibitors (any) plus inflammatory arthritis (to include RA, PsA, seronegative arthritis, spondyloarthritis)
3.2.3.1.3. Rituximab in patients with AAV
3.2.3.2. Serology Group:
3.2.3.2.1. Methotrexate plus:
3.2.3.2.1.1. inflammatory arthritis (RA, seronegative arthritis and PsA)
3.2.3.2.1.2. psoriasis
3.2.3.2.2. TNF inhibitors (any) plus:
3.2.3.2.2.1. inflammatory arthritis (RA, seronegative arthritis, axSpA and PsA)
3.2.3.2.2.2. psoriasis
3.2.3.2.2.3. Crohn's disease
3.2.3.2.3. IL-17 inhibitors (any), IL-12/23 inhibitors and IL-23 inhibitors plus:
3.2.3.2.3.1. seronegative arthritis (PsA and axSpA)
3.2.3.2.3.2. psoriasis
3.2.3.2.4. IL-6 inhibitors (any) with RA
3.2.3.2.5. JAK inhibitors (any) with RA
3.2.3.2.6. Rituximab with RA or AAV
3.2.3.2.7. Any immune modifying treatment with Systemic Lupus Erythematosus (SLE)
3.2.3.3. Serology Plus Group: aged 5 to <18 years at time of recruitment and
3.2.3.3.1. Methotrexate plus inflammatory arthritis with onset under the age of 16 years (also known as juvenile idiopathic arthritis JIA), with or without JIA-uveitis
3.2.3.3.2. TNF inhibitors (any) plus inflammatory arthritis with onset under the age of 16 years (JIA), with or without JIA-uveitis
3.2.3.3.3. IL-6 inhibitors (any) plus inflammatory arthritis with onset under the age of 16 years (JIA), with or without JIA-uveitis
3.2.3.3.4. Any immune modifying treatment with juvenile onset Systemic Lupus Erythematosus (JSLE)
3.2.3.3.5. Rituximab with plus inflammatory arthritis with onset under the age of 16 years (JIA), with or without JIA-uveitis or AAV
3.3. Diagnosed with the following chronic renal conditions:
3.3.1. End stage kidney disease secondary to any cause
3.3.2. Renal transplant following end stage kidney disease
3.4. Diagnosed with the following chronic liver conditions:
3.4.1. Liver cirrhosis
3.4.2. Liver transplantation
3.4.3. Chronic liver disease (of any stage), or gastrointestinal disease on immune suppressive therapy
3.5. Haematopoietic stem cell transplant patients:
3.5.1. Previously treated with autologous or allo-HSCT for any indication and with any conditioning regimens and intensities
3.5.2. Previously treated with CAR-T cell therapies
Note: HSCT and CAR-T recipients who have received one or two doses of a SARS-CoV-2 vaccine pre-procedure and are receiving re-vaccination post HSCT / CART-T are eligible for recruitment at:-
3.5.2.1. Baseline (prior to re-vaccination dose 1) to either Deep Immunophenotyping Group or Serology Group

3.5.2.2. For the Deep Immunophenotyping Group: before they received the second re-vaccination dose (booster)
3.5.2.3. For the Serology Group: up to 28 (-7 /+ 56) days post second re-vaccination (booster) only if 2 doses have been administered post-HSCT / CAR-T procedure.
3.6. Post solid organ transplant in 5 to <18 year olds to the Serology Plus group
3.6.1. Post heart, lung, heart-lung, or kidney transplantation and on immune suppressing medication (calcineurin or mTOR inhibitor, plus additional agents)

Previous inclusion criteria:
1. Are eligible for vaccination by one of the SARS-CoV-2 vaccines approved by the MHRA administered in accordance with the UK Government's COVID-19: the green book, chapter 14a and have either:
1.1. Not received the first dose of the vaccine
Or
1.2. Have participated in a study where bloods were taken prior to their first dose of vaccine and the blood samples were stored and are available for analysis in OCTAVE trial
2. Anticipated life expectancy of 6 months or greater
3. Fall into one (or more) of the following patient cohorts who will meet disease relevant classification, disease state, and staging according to established international standards:
3.1. Diagnosed with any of the following malignancies:
3.1.1. Breast
3.1.2. Lung
3.1.3. Acute Myeloid Leukaemia
3.1.4. Multiple Myeloma
3.2. Diagnosed with the following rheumatic/inflammatory conditions:
3.2.1. Specialist diagnosis of relevant condition
3.2.2. Established on relevant therapy for ≥ 30 days
3.3. Meet the definitions in any of the following cohorts:
3.3.1.The deeply immunophenotyped cohorts:
3.3.1.1. Methotrexate in patients with RA
3.3.1.2. TNF inhibitors (any) in patients with RA
3.3.1.3. Rituximab in patients with AAV
3.3.2. Treatment cohorts:
3.3.2.1. Methotrexate plus:
a) inflammatory arthritis (RA and psoriatic arthritis (PsA))
b) psoriasis but no inflammatory arthritis
3.3.2.2. TNF inhibitors (any) plus:
a) inflammatory arthritis (RA and PsA)
b) psoriasis but no inflammatory arthritis
c) Crohn's disease but no inflammatory arthritis
3.3.2.3. IL-17 inhibitors (any) plus:
a) seronegative arthritis (PsA and axSpA)
b) psoriasis but no inflammatory arthritis
3.3.2.4. IL-6 inhibitors (any) with RA
3.3.2.5. JAK inhibitors (any) with RA
3.3.3. Diagnosed with the following chronic renal conditions:
3.3.3.1. End stage kidney disease secondary to any cause
3.3.3.2. Renal transplant following end stage kidney disease
3.3.4. Diagnosed with the following chronic liver conditions:
3.3.4.1. Liver cirrhosis
3.3.4.2. Liver transplantation
3.3.4.3. Chronic liver disease (of any stage), or gastrointestinal disease on immune suppressive

therapy
3.3.5. Haemopoietic stem cell transplant patients:
3.3.5.1. Previously treated with autologous or allo-HSCT for any indication and with any conditioning regimens and intensities
3.3.5.2. Previously treated with CAR-T cell therapies

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
750 deep immunophenotyping group; 4,250 serology group; 160 serology plus group

Total final enrolment
2812

Key exclusion criteria
Have already received the first dose of the vaccine and have not participated in a study where blood samples taken prior to their first dose of vaccine were stored and are available for analysis in OCTAVE trial

Date of first enrolment
22/02/2021

Date of final enrolment
31/07/2022

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Glasgow Royal Infirmary
NHS Greater Glasgow and Clyde
Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
St. James's University Hospital
Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Hammersmith Hospital
Imperial College Healthcare NHS Trust
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
King's College Hospital
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Royal Hallamshire Hospital
Sheffield Teaching Hospitals NHS Foundation Trust
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Study participating centre
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Cranmer Terrace
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SW17 0QT

Study participating centre
Freeman Hospital
Freeman Road
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United Kingdom
NE7 7DN

Study participating centre

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Sponsor type
University/education

Website
http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

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
The trial results will be submitted for publication in a high-impact peer-reviewed journal. The manuscripts will be prepared by the Trial Management Group (TMG) and authorship will be on behalf of the collaborative group.
The results of the trial will be published on public registries and a lay summary of the results provided for participants on the trial website.

Intention to publish date
30/06/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
Requests may be received to share the trial data and research samples collected with researchers running other studies in this and other organisations so that they may perform analysis on the data to answer other important questions about vaccination for coronavirus. Such organisations may include universities, NHS and Public Health England or companies involved in health research and may be in this country or abroad. Requests for data to be shared will be approved by the CRCTU senior Management, as per CRCTU Data Sharing Policy, and will only be granted if the necessary procedures and approvals are in place. Any data shared with other researchers will be anonymised.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Preprint results		23/08/2021	31/08/2021	No	No
HRA research summary			28/06/2023	No	No
Results article	version 1.0	10/07/2023	24/07/2023	Yes	No
Results article	adult cohorts	06/07/2023	24/07/2023	Yes	No
Protocol file	version 9.0	15/03/2022	14/11/2024	No	No
Plain English results			30/06/2025	No	Yes