UK Health Security Agency

COVID-19 CONSENSUS study protocol

Contents

Study information

An audit of the antibody levels and T cell responses following the extended COVID-19 vaccine schedule currently used in the UK's National Immunisation Programme

Short Title: COVID-19 VacciNe reSponses after Extended immuNisation SchedUleS (CONSENSUS)

PHE R&D REGG Ref	NR0253
Protocol version:	10.0
Date:	26 November 2021
Sponsor:	UK Health Security Agency, Wellington House 133-155 Waterloo Road, London SE1 8UG
Chief investigator:	Dr Gayatri Amirthalingam
Co-investigators:	Dr Sathyavani Subbarao, Dr Kevin Brown, Dr Shamez Ladhani, Dr Mary Ramsay, Dr Frances Baawuah, Dr Paul Moss (University of Birmingham)

1. Amendment history

Amendment number.	Protocol version	Date issued	Author(s) of changes	Details of changes made
1	2.0	16/01/2021	GA	Responding to REGG review comments received on 14/01/2021.
2	3.0	18/01/2021	SS	Responding to REGG review comments received on 18/01/2021 Responding to changes requested by deputy chief medical officer.
3	4.0	27/01/2021	SS	The consent form has been updated to reflect and align with the consent procedure in the protocol in order to access relevant medial history. Participant questionnaire format has been modified including amending question on occupation.
4	5.0	23/02/2021	SS	Recruitment has been updated to include adults over 50 years, increase the number of participants to 120 per 10 year age-band and to extend recruitment up to 6 weeks after the first dose.
5	6.0	27/04/2021	SS	To reflect the sampling at 15 weeks and not at the time of the second vaccine. To increase recruitment at 7 weeks. To add a questionnaire at 15 weeks to capture missing vaccine symptom.
6	7.0	17/08/2021	GI/GA	To reflect sampling changes to include monitoring for potential introduction of a booster vaccination programme/s and to include information about Tasso devises.
7	8.0	17/09/2021	GI	To include a question on flu vaccination history.
8	9.0	19/11/2021	GI	To extended recruitment of monitoring of post-booster vaccine.
9	10.0	26/11/2021	GI	To include the recruitment of Moderna booster participants from the National Immunisations Management Service.

2. Introduction

The SARS-CoV-2 pandemic has accelerated vaccine development, particularly with novel platforms, some of which builds upon work with previous SARS-CoV vaccines and other viral vaccine technologies. Doses for several promising candidates have been secured by the UK government in advance of completion significant efficacy in human trials (1, 2). The MHRA has approved use of 3 vaccines; (1) Pfizer BioNTech COVID-19; (2) AstraZeneca COVID-19 vaccines; and (3) COVID-19 Moderna vaccine. Currently 2 of these vaccines, the Pfizer BioNTech COVID-19 and Astra-Zeneca COVID-19 vaccines have been deployed for use in the national programme. These vaccines products are currently being deployed as a 2-dose schedule.

The first vaccine licensed in the UK, from Pfizer BioNTech is a nucleoside modified mRNA vaccine encoding the full-length SARS-CoV-2 spike protein. Initial phase 1 efficacy studies examined the prime-boost approach 21 days apart evaluating several prime dose concentrations (12 participants in each cohort). Sera samples were taken at baseline, at days 7, 21 after the priming dose and then 7, 21, 28 and 63 days after the boosting dose. Pfizer BioNTech COVID-19 elicited a strong neutralising antibody response (also robust anti-Spike 1 and Receptor Binding Domain responses) 21 days after the priming with all dose concentrations. Following the boost at 21 days, further sera was taken 7 days later (day 29) and showed increased neutralising responses which were sustained 63 days (day 85) after the booster. In 32 of 34 participants, cellular assays were performed 7 days after the boosting dose and showed proliferation of antigen specific CD4+ and CD8+ T-cell compared to the baseline titres (3). Furthermore, Pfizer BioNTech COVID-19 vaccine-elicited sera was able to neutralise pseudovirus with a range of SARS-CoV-2 variants suggesting robust cross-neutralisation in the presence of novel variants. In phase 2/3 trials of 43,548 adult participants (total), the Pfizer BioNTech COVID-19 vaccine was administered in the same prime-boost schedule with 2 doses administered at 21 days apart (1). The primary end-point was confirmed COVID-19 infection at least 7 days after the second dose. The efficacy of the 2-dose regimen was estimated at 95% against confirmed COVID-19 infection.

AstraZeneca COVID-19 vaccine utilises a simian adenovirus vector that expresses the spike protein (4). In a phase 1 single-blind randomised control trial of 1,077 healthy adults, a single dose regimen and a prime-boost regimen was compared against a group receiving the MenACWY vaccine. Sera was taken at baseline, 7, 14, 28 and 56 days following the first vaccine and in the prime boost group, additional sera were collected at 35 and 42 days post first vaccine dose. Spike specific IgG responses rose at day 28 and was sustained at day 56. In the prime boost group, Spike IgG continued to rise following the 28 day second boost. Neutralising antibody was assessed at baseline, day 14, 28 and 56, with the additional day 35 and 42 time points for the prime-boost group. Responses were 91% in the single dose group at day 28 and 100% in the prime-boost group (4). Cellular assays were also performed at 0, 7, 14, 28 and 56 days (with a further sample at day 35 for the prime-boost group). Spike specific T cell responses peaked at 14 days (for both the single dose and prime-boost regimens) and declined at day 56 after vaccination. In a multi-centre and multi-national

phase 2/3 trial (23,848 enrolled and 11,636 reported in the primary efficacy analysis) assessing primary efficacy of the 2 dose regimen, participants were assigned to AstraZeneca COVID-19 vaccine (with a subset receiving a half-dose formulation as their 'prime' regimen) or a control (MenACWY). The prime-boost regimen was initially designed with the second dose at 4 weeks; however, changes in the protocol meant the second dose was given after the initial proposed time-point (with approximately 53.2% of those in the UK, low prime dose arm receiving the second dose 12 weeks after the first). Vaccine efficacy was between 62.1% (full-dosing) and 90% (in the lower dose sub-group)(2). There were 10 hospitalisations, all of whom were in the control arm.

In the UK the top priority groups in Phase 1 deployment include care home residents and staff, frontline healthcare workers and older adults. The vaccine is offered through NHS Hospital Trusts, mass vaccination hubs and general practice. The licensed recommended schedule is for the second dose of vaccine to be given at 3 weeks (Pfizer BioNTech) and from 4 to 12 weeks (AstraZeneca vaccine) after the first dose.

UK Health Security Agency (UKHSA) is responsible for the evaluation of the national immunisation programme and undertakes enhanced surveillance of vaccine preventable diseases to monitor vaccine impact and effectiveness. Authorisation for the Pfizer BioNTech vaccine is based on a 2-dose schedule administered 21 days apart and, for the Oxford AstraZeneca vaccine, 4 to 12 weeks after the first dose. However, given the UK COVID-19 epidemiology in late 2020 with rapid increase in cases, hospitalisation and deaths along with the emergence of a highly transmissible variant strain, there was a need for rapid, high uptake of the COVID-19 vaccine uptake amongst vulnerable persons. On 30 December 2020, therefore, the UK expert advisory immunisation committee, the Joint Committee on Vaccination and Immunisation (JCVI) published updated advice to extend the interval between the first and second doses to up to 12 weeks for both vaccines so that as many people within the priority groups for Phase 1 can be vaccinated quickly with at least 1 dose. A single dose is expected to provide adequate protection until the second dose is given to provide more long-term protection. With most vaccines, an extended interval between the prime and booster doses leads to a better long-term immune response. There is good evidence that extending the intervals between doses of hepatitis B, hepatitis A and HPV vaccines provide better immune responses at follow up. For example, whilst an accelerated schedule for hepatitis B, with immunisation at 0, 1 and 2 months, will confer protection more quickly and is expected to provide better patient compliance. With such an accelerated schedule, a fourth dose at 12 months is required to assure long term protection as antibody concentrations after the third dose are lower than those obtained with the 0, 1, 6 months schedule (6, 7).

Whilst there is some data through the trials for the AstraZeneca vaccine using extended schedules, this is far more limited for the Pfizer BioNTech COVID-19 vaccine, particularly for those in the oldest age groups. Given the critical importance in evaluating the persistence of antibody levels in those who have received the extended schedule currently being deployed in the UK, UKHSA is initiating a rapid audit to measure and compare antibody and cellular responses to COVID-19 vaccines using extended schedules with individuals who received 2

doses 21 days apart before the change in UK Government advice. This has been deemed by the Deputy Chief Medical Officer and DHSC as a high national public health priority to provide reassurance that individuals receiving this extended schedule (outside of the authorised approval by regulators) are retaining their antibody levels until they receive their second dose up to 12 weeks later. Furthermore, by testing samples on multiple assays, this information will also be used to interpret the ongoing sero-surveillance activities being undertaken by UKHSA.

This audit has been identified as a national public health priority the findings will be rapidly shared with JCVI and policy makers to inform any changes required to the current UK strategy.

Following the JCVI interim advice in June 2021 that a potential booster programme should be considered from September 2021, starting with those most at risk of serious disease, the audit will be extended to incorporate the monitoring of this programme in CONSENSUS participants.(8) It has since been announced that people aged 40 years and over will be eligible for boosting with a third dose (booster) with either a single dose of BNT162b2 or a half dose (50µg) of Moderna (mRNA-1273/Spikevax®) vaccine.

3. Overall aim

To compare the antibody and T cell responses in adults receiving COVID-19 vaccine, as part of the current UK vaccination programme using a 2-dose schedule of up to 12 weeks apart compared with the authorised schedule, and additional booster doses.

3.1 Key outcomes of interest

For both groups, the key outcomes of interest are:

- antibody responses following first, second and booster dose of COVID-19 vaccines
- T cell responses following first, second and booster dose of COVID-19 vaccines
- kinetics and profile of antibody and T cell responses between vaccine types
- kinetics and profile of antibody and T cell responses by age
- kinetics and profile of antibody and T cell responses in naïve and previously infected individuals

4. Sites, recruitment and eligibility

4.1 Recruitment

This is a prospective longitudinal audit of adults receiving COVID-19 vaccine as part of the current national immunisation programme in England. Potential participants will be recruited through NHS hospitals and General Practices in England. We aim to recruit a minimum of 120 participants in 10-year age bands in adults over 50 years and prioritising those over 60 years old. Participants receiving an extended schedule of either the Pfizer BioNTech or AstraZeneca COVID-19 vaccines will be followed up with serial samples requested over 24 months. Individuals who are invited to attend their first COVID-19 vaccines will be provided with information about the audit and offered the opportunity to take part. This group will be compared with a comparator group of vaccinated individuals who have previously received the 2-dose schedule according to the authorisation prior to the change in UK policy. They will be recruited within 3 weeks of receiving their second vaccine dose. All participants will have the opportunity to ask questions about the audit and provide written informed consent before taking part.

Additional participants will be recruited to enable the evaluation of the Moderna booster dose. There are 2 pathways that may be used to recruit participants boosted with the Moderna vaccine, firstly, in-person enrolment from GP and vaccine sites delivering Moderna booster doses, and, secondly, via the National Immunisation Management Service (NIMS). UKHSA will preferably enrol participants via the first enrolment route, but if numbers are insufficient or we are unable to get permission to recruit directly from the sites administering Moderna vaccine we will recruit via the second route. Via the second recruitment method, we will use the electronic NIMS, which maintains a record of all COVID-19 vaccinations in England and is updated regularly, to identify participants.

UKHSA will contact potential participants around 1 week after their booster dose and provide them with information about the evaluation via a telephone call or Notify email or text message. UKHSA will only contact participants aged 50 years old and older, living within North Central London CCG, are not flagged as Clinically Extremely Vulnerable or Immunosuppressed and where the booster dose is 6+ months after the second primary dose. Participants who express an interest will be asked to provide preliminary consent using a secure online SnapSurvey platform, which is held at UKHSA Colindale, and contact information. Participants who express interest in taking part will be contacted and invited to a blood sampling day 3 to 4 weeks after booster dose, after which they would resume on the post-booster testing schedule. Once at the sampling site, participants will again be provided with the information leaflet again and asked to sign a consent form.

4.2 Subject eligibility

4.2.1 Inclusion criteria

Adults aged at least 50 years who are invited to receive a COVID-19 vaccine as part of the national immunisation programme in England and are able to provide informed written consent, and either:

- individuals who receive the first dose of a COVID-19 vaccine and have their first visit blood sample within 72 hours of vaccination and/or are within 21 days of their first COVID-19 vaccine
- individuals who have received 2 doses of Pfizer BioNTech COVID-19 vaccine with a vaccine interval of 21 days, and are enrolled within 21 days of the second dose (comparator arm)
- we will also include individuals who are up to 7 weeks post their first dose of vaccination
- to ensure adequate numbers for analysis of the booster vaccine audit, we will also include individuals who are up to 4 weeks post-booster vaccine

4.2.2 Exclusion criteria:

- individuals who have previously taken part in a COVID-19 vaccine trial
- individuals who are unable to provide informed written consent
- individuals who are less than 50 years of age
- individuals who are immunosuppressed (as defined in the Green Book)

4.2.3 Temporary exclusion criteria

None

4.3 Procedures

4.3.1 Questionnaires and blood sampling:

Consenting participants will be asked to complete a short questionnaire about their health and a blood sample will be taken.

The blood samples will be taken where possible by experienced staff and/or a dedicated phlebotomist at each site. Around 10 to 20 ml of blood will be taken by venepuncture at each sample collection point. If the patient is not able to visit at a time where there is a dedicated phlebotomist available some patients may be sent a self-sampling kit (Tasso Inc) to obtain 200 to 400 ul of capillary blood for serological testing only.

In a subset of participants (less than 50%), following appropriate written informed consent, additional blood (lithium heparin sample, 10 to 30mls) will be taken during some of the visits (typically 0, 3 weeks and 6 weeks, 9 weeks, 12 weeks, 5 to 6 months after first dose, 12 months and 24 months after vaccine dose 1. In participants who have received a booster-vaccine and consented to the booster-testing schedule, it typically will include pre-first booster, 3 weeks post first booster, 3 months, 6 months, 12 months and 18 months post booster. If second boosters are approved nationally, testing times will typically include, pre second booster (if advised), 3 weeks post second booster, 18 months and 24 months.

All samples will be labelled with the participant's ID number, sex, date of birth, and the date of sample.

The blood samples will be appropriately packed and sent by Hayes Courier Service or courier service to UKHSA, where they will be processed and stored until they are batch-tested for coronavirus antibodies. Samples for cellular studies will be sent directly to the specialist testing laboratory (Oxford Immunotech).

4.3.2 Sample packaging and transport

Samples are collected and placed into a NOAX tube. The Noax tubes are placed in UN3373 compliant packaging and transported by an approved courier to their secure destination. These services are trackable.

4.3.3 Subsequent visits

For the monitoring of doses 1 and 2:

Main (audit) group: The participant will then be invited (by phone, text and/or email according to their preference) to have additional blood samples as follows (approximately 2 weeks for each visit).

The sampling will therefore be as follows:

Visit 1: day 0 (dose 1 of COVID-19 vaccine) approximately 3 days

Visit 2: 3 weeks after first vaccine dose

Visit 3: 6 weeks after first vaccine dose

Visit 4: 9 weeks after first vaccine dose

Visit 5: 12 weeks after first vaccine dose

Visit 6: 15 weeks after first vaccine dose

Visit 7: 20 weeks after first vaccine dose

Visit 8: 6 months after first vaccine dose

Visit 9: 18 months after first vaccine dose

Visit 10: 24 months after first vaccine dose

Comparator group (receiving authorised schedule):

A group of 120 participants who have received their second dose schedule of the Pfizer BioNTech COVID-19 vaccine (21 day interval) will be invited (by phone, text and/or email according to their preference) to take bloods 3 weeks after the second vaccine dose and bloods to be taken thereafter as above:

Visit 1: 3 weeks after the second vaccine (approximately 6 weeks after the first vaccine dose)

Visit 2: 6 months after first vaccine dose

Visit 3: 12 months after first vaccine dose

Visit 4: 24 months after first vaccine dose

For the monitoring of a potential booster vaccination programme:

JCVI have indicated that a booster programme will be implemented for those at higher risk in September 2021. In participants who receive a booster vaccine and consent to testing, monitoring of the booster programme will replace the existing sampling schedule will be as follows:

Visit 1: September 2021 to test for pre-booster antibodies

Visit 2: 4 to 6 weeks after booster dose

Visit 3: 3 months after booster dose

Visit 4: 6 months after booster dose

Visit 5: 12 months after booster dose

Subject to JCVI decisions on further booster doses participants will be tested as follows:

- no additional booster programme:
    - visit 6: 18 months after booster dose
- additional booster programme implemented:
    - visit 6: 4 to 6 weeks after booster second dose
    - visit 7: 3 months after booster second dose
- if participants are unable to attend their blood sampling visit, arrangements may be made with the participant's permission for the blood sampling to be performed at the participant's residence by a trained member of the evaluation staff
- in the event that there are not sufficient numbers of participants within the study to evaluate the available combinations of primary and booster vaccine types, more participants will be recruited, a maximum of 4 weeks after booster-vaccine

- alternatively, with the permission of the patient if the patient is not able to visit at a time where there is a dedicated phlebotomist available some patients may be sent a self-sampling kit (Tasso Inc) to obtain 200 to 400 ul of capillary blood for serological testing only
- participants who miss 1 appointment will continue to be asked to attend subsequent appointments
- participants will be asked to complete a short questionnaire at each of the visits
- participants who develop COVID-19 symptoms at any time during the evaluation will be asked to contact UKHSA and a self-test swab kit will be sent to their home to be returned to UKHSA to test for SARS-CoV-2 infection

4.3.4 Testing samples

Sera will be separated on arrival at Sero Epidemiology Unit, UKHSA, divided into aliquots and frozen at -30ºC or below.

Blood samples will be tested for coronavirus antibodies (N, RBD and S) in the same laboratory using the same methodology throughout the surveillance.

Any remaining serum samples at the end of the audit will be anonymised and incorporated into the UKHSA Sero-epidemiology Unit collection (Ethics application number 05/Q0505/45) if permission for this has been granted by the participant; otherwise they will be destroyed.

A subset of the samples will be tested for neutralising antibodies.

Additional blood samples taken in a subset of participants (lithium heparin whole blood 10 to 30 mls which will be tested for T cell and B cell immunity. These samples will need to remain at room temperature and assays performed within 32 hours of sampling.

4.3.5 Data entry, analysis and presentation

The audit will be co-ordinated by UKHSA Immunisation and Countermeasures Division at Colindale, where all data will be held and analysed. The overall results will be reported to relevant authorities in UKHSA, the JCVI and the Department of Health. A paper containing the overall results of the antibody testing will be submitted for publication in a peer-reviewed journal. It will not be possible to identify any individual participant or individual results in any of the reports or publications.

4.3.6 Withdrawal of participants

Participants will be able to withdraw consent for participation at any time without prejudice and without giving a reason by contacting the UKHSA team. However, where a reason is provided, this will be recorded. A member of the audit team can withdraw a subject if, in their clinical judgment, it is in the best interest of the subject or if the subject cannot comply with the protocol.

4.3.7 Expenses and payments

It is not expected that the participants will incur any costs. If they do occur, however, then any costs incurred by the participants for attending the appointments can be reimbursed upon request.

5. Number of subjects and duration

This is an audit of a rapidly implemented national programme in response to a global pandemic, using an extended immunisation schedule with a longer interval between doses than licensed for multiple COVID-19 vaccines. We plan to recruit a minimum of 120 participants for each group under investigation for the currently licensed vaccines in the national immunisation programme. These groups are adults over 50 years and include 120 participants at 10 year age bands, prioritising 60+ year olds.

5.1 Sample size calculation

The geometric mean responses and declines in each of the groups will be calculated. We will calculate the geometric mean ratio of responses between the groups with a 95% confidence interval which allows non-inferiority to be assessed.

We will also perform this analysis after adjusting for covariates (age, comorbidities, sex, ethnicity) in a multivariable regression model on logged data. Responses to natural infection in the 2 to 6 week period as measured by the RBD assay gives a geometric mean response of 28 units and a standard deviation on a log-10 scale of 0.5. Using this standard deviation as a conservative high estimate of the variability post vaccination then a sample size of at least 220 per group when comparing post second dose levels has 90% power at 5% 2 sided (2.5% 1 sided) significance level for a non-inferiority margin of 30% (for .example if GMT is 28 in 1 group then not less than 0.7*28 = 19.6 in the other group).

6. Compliance with guidelines

As a public health body, UKHSA data collection role is strictly governed. All data will be collected and handled in accordance with UKHSA guidelines and policy:

- recommendations of the UKHSA Caldicott committee
- General Data Protection Act (GDPR)
- Human Rights Act
- Section 3 of the Health Service Regulations 2002

7. Ethical approval

This audit is being undertaken by UKHSA under Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002 which states:

7.1 Communicable disease and other risks to public health

1. Subject to paragraphs (2) and (3) and regulation 7, confidential patient information may be processed with a view to:

    a) diagnosing communicable diseases and other risks to public health
    b) recognising trends in such diseases and risks
    c) controlling and preventing the spread of such diseases and risks
    d) monitoring and managing:
        i. outbreaks of communicable disease
        ii. incidents of exposure to communicable disease
        iii. the delivery, efficacy and safety of immunisation programmes
        iv. adverse reactions to vaccines and medicines
        v. risks of infection acquired from food or the environment (including water supplies)
        vi. (the giving of information to persons about the diagnosis of communicable disease and risks of acquiring such disease

2. For the purposes of this regulation, “processing” includes any operations, or set of operations set out in regulation 2(2) which are undertaken for the purposes set out in paragraph (1).
3. The processing of confidential patient information for the purposes specified in paragraph (1) may be undertaken by—

    a) the UKHSA Laboratory Service
    b) persons employed or engaged for the purposes of the health service
    c) other persons employed or engaged by a government department or other public authority in communicable disease surveillance

UKHSA Research and Development and the sponsors were consulted and confirmed that the work would be covered as an audit and hence does not require external research ethics approval.

7.2 Participant confidentiality

Personal data collected for the purposes of this audit may include name, date of birth, address as well as the blood test results and any relevant medical information required to assess antibody responses. For access to patient electronic records, EMIS will also be sought in order to ascertain vaccination dates, relevant medical history and basic patient demographics. The only people with access to this information will be the audit team, or regulatory authorities who may wish to check the audit is being carried out according to appropriate guidelines. Every effort will be made to protect the participants' identity. Data will only be used for the purposes of this audit stored in secure UKHSA facilities with restricted access and destroyed 3 years after the end of the project.

8. Target dates

- recruitment to commence: 18 January 2021
- completion of recruitment: 12 months after first recruitment
- completion of audit: 3 years after first recruitment

9. References

1. Polack FP and others. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. New England Journal of Medicine, 2020.
2. Voysey M and others. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet, 2021.
3. Sahin U and others. BNT162b2 induces SARS-CoV-2-neutralising antibodies and T cells in humans. Preprint. 2020.
4. Folegatti PM and others. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet, 2020.
5. Baden LR and others. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. New England Journal of Medicine, 2021.
6. Schönberger K and others. Determinants of long-term protection after hepatitis B vaccination in infancy: a meta-analysis. Pediatric Infectious Disease Journal, 2013
7. Mangione R and others. Delayed third hepatitis B vaccine dose and immune response. Lancet, 1995.
8. UK Health Security Agency. 2021. Press Release: JCVI issues interim advice on COVID-19 booster vaccination.

Appendix 1: Information leaflet for dose 1 and 2 follow-up extended schedule

Information leaflet for participants

COVID-19 Vaccine Responses after extended immunisation schedules

Consensus (version 6, 30 April 2021)

We would like you to invite you to take part in a national audit of the extended COVID-19 vaccine immunisation schedule that is recommended in the UK. One of the current COVID-19 vaccines are licensed to be given 3 weeks apart. Extending the interval between the 2 vaccine doses to 12 weeks for all available COVID-19 vaccines, allows many more people to receive at least one dose of vaccine.

We are able to recruit you anytime between the day of the first vaccine dose and 6 weeks after this. We want to check the antibody levels provided by the first dose of vaccine until the second dose and up to 24 months later. Depending on at what time-point you have joined our audit, this will involve having a blood test at the following times:

- when you receive the first dose of vaccine (if you enrol at the time of your first vaccine dose)
- approximately 3 weeks after first vaccine dose (if you enrol either at time of first vaccine dose / 3 weeks after first vaccine dose)
- approximately 6, 9 and 12 weeks after the first vaccine dose (all participants)
- 3 weeks after the second dose and 6, 12 and 24 months after the first dose of vaccine (all participants)

So, the maximum number of blood tests could be 9, but this will be lower if we have recruited you after your first vaccine dose. Before you decide to take part, we would like you to understand why we are doing this, and what it would involve. Please ask us if there is anything that is not clear.

Why we are doing this audit

UK Health Security Agency (UKHSA) is undertaking this audit to assess the antibody levels offered by the extended 12 week schedule that is currently recommended in the UK for COVID-19 vaccines. We are looking for volunteers who are due their COVID-19 vaccine to provide blood samples from the time of their first vaccination until 24 months after their first dose of vaccine to measure the immunity provided by COVID-19 vaccine. There is currently limited data for this given the pace at which the vaccine has been rolled out, so this is really very important.

We will use the blood samples to measure antibodies provided by the COVID-19 vaccine against the novel coronavirus, SARS-CoV-2. For some participants, we may also ask to take some extra blood as some of the visits for additional cellular immunity tests (T cell and B cell immunity).

The results of the blood tests will provide important information about the level of immunity provided by the first dose until the second dose and for up to 2 years later. We would like to include a range of people who are eligible for the COVID-19 vaccine, depending on their age, underlying medical problems, and whether they have had COVID-19 in the past.

Why you have I been asked to take part

You have been asked to take part because you are one of the first people to be offered the COVID-19 vaccine. We have limited data on the long-term level antibody levels provided by the vaccine, and the results of yours and other participants' blood tests will be used to inform public health guidance and recommendations on the need for future COVID-19 vaccinations

Donating the blood sample is voluntary - it is up to you to decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form.

What we want you to do

If you decide to take part, we will arrange the following visits with you:

- visit 1: when the first dose of COVID-19 vaccine is given
- visit 2: 3 weeks after the first dose of the vaccine
- visit 3: 6 weeks after the first dose of vaccine
- visit 4: 9 weeks after the first dose of vaccine
- visit 5: 15 weeks after the first dose of vaccine
- visit 6: 6 months after the first dose of vaccine
- visit 7: 12 months after the first dose of vaccine
- visit 8: 24 months after the first dose of vaccine

COVID-19 vaccination

You will receive your first dose of COVID-19 vaccine at recruitment (visit 1)

You should receive your second dose of vaccine at approximately 12 weeks later The timing of vaccination may vary depending on vaccine availability and when your local centre contacts you for vaccination.

Blood sampling visits

At each visit, you will be asked to complete a short questionnaire and provide a blood sample.

Around 10 to 20 mls of blood (about 1 tablespoon) will be taken by a trained member of staff or a phlebotomist. For some participants, we will ask permission to take some more blood (15 to 30 ml, or 1 to 2 tablespoons) during some of the visits to test for cellular immunity.

For each visit, we will arrange the blood sampling to be done at a time and place that is convenient to you. This may be at your GP surgery, the local blood testing centre or at your home.

For each visit, the blood sample may be taken up to a week before or after the planned visit date.

If a blood sampling visit is missed, you can still continue to take part.

What will happen to your samples

Your blood samples will be sent to UKHSA, processed and stored with other samples until they are all tested together for SARS-CoV-2 antibodies. Any additional blood sample we collect will be sent to a specialist laboratory to test for cellular immunity. With your permission, we would like to store any remaining blood sample at UKHSA so that we may use for future test to understand virus infections and immunity. The samples will be stored anonymously and it will not be possible to link the sample back to you. You can choose what happens to any remaining samples on the consent form. You can still take part even if you ask us to have the blood sample destroyed after the tests are complete.

Taking part in this audit will be confidential

We will need to collect some personal information, including your name, date of birth, contact details and health information to help us understand the results of the tests that we perform and to contact you for future appointments. We will also need to access your electronic GP records in order to ascertain the dates when your vaccines have been given.

We will keep all the information securely as we do for all the tests we perform at UKHSA. We will write our reports in a way that no one can work out that you took part in the audit. All personal data will be stored in accordance with the General Data Protection Regulations (GDPR) and the Data Protection Act 2018.

What the benefits are to you

This important audit will not benefit you directly, but your participation will support national immunisation policy to help better protect and improve health and well-being of the population. At the end of the audit, the overall results will be published in a UKHSA report, and we can provide you with a copy if you wish.

What the disadvantages are

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 light headedness when the blood is drawn, and rarely, an infection at the site of the blood draw.

If you change your mind

If you no longer want to be involved, you can withdraw from the audit at any time and without giving a reason by contacting the UKHSA team (telephone (0208 495 3240) or email (Consensus@phe.gov.uk)).

What you should do now

If you would like to take part, please complete and sign the consent form. If you have any questions about the taking of the blood samples or any other questions about the audit, please do not hesitate to ask the team (telephone (0208 495 3240) or email (Consensus@phe.gov.uk)) between Monday – Friday 9am to 5pm.

Who has reviewed the audit

This work has been reviewed by UKHSA Research and Development team and the UKHSA Research Ethics and Governance of public health practice Group (UKHSA REGG).

What to do if you have any concerns

If you have any concerns, please talk to a member of the team. If you are still unhappy, you can contact the UKHSA Research and Development (R&D) Team (RandD.OFFICE@phe.gov.uk).

Funding

This audit is being supported by UKHSA and the Department of Health and Social Care

Extra costs incurred

If there are extra expenses are incurred in addition to the vaccination visits, these can be claimed back from UKHSA.

Appendix 2 : Information leaflet for dose 1 and 2 follow-up comparator group

Information leaflet for participants

COVID-19 Vaccine Responses in participants receiving the standard immunisation schedule

CONSENSUS (version 6, 30 April 2021)

We would like you to invite you to take part in a national audit of the COVID-19 vaccine immunisation schedule that is recommended in the UK. One of the current COVID-19 vaccines are licensed to be given 3 weeks apart.

We understand you have received 2 doses of the Pfizer BioNTech vaccine and would like to check your antibody levels 3 weeks after your second vaccine dose and up to 24 months later. This will involve having a blood test at 4 time periods including at 3 weeks after the second dose and at 6 and 12 and 24 months after the first dose of vaccine. Before you decide to take part, we would like you to understand why we are doing this, and what it would involve for you. Please ask us if there is anything that is not clear.

Why we are doing this audit

UK Health Security Agency (UKHSA) is undertaking this audit to assess the antibody levels offered by the standard 3 week schedule compared with the current UK schedule.

If you agree to take part, we will use the blood samples to measure antibodies provided by the vaccine against the novel coronavirus, SARS-CoV-2. For some participants, we may also ask to take some extra blood as some of the visits for additional cellular immunity tests (T cell and B cell immunity).

The results of the blood tests will provide important information about the level of immunity provided by the second dose and for up to 2 year later. We would like to include a range of people who are eligible for the COVID-19 vaccine, depending on their age, underlying medical problems, and whether they have had COVID-19 infection in the past

Why you have been asked to take part

You have been asked to take part because you are one of the first people to be offered the COVID-19 vaccine. We have limited data on the long-term level of immunity provided by the vaccine.

Donating the blood sample is voluntary - it is up to you to decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form.

What we want you to do

If you decide to take part, we will arrange the following visits with you:

- visit 1: 3 weeks after the second vaccine dose has been given (this will also be around 6 weeks after the first vaccine dose)
- visit 2: 24 weeks (6 months) after the first dose of vaccine
- visit 3: 52 weeks (12 months) after the first dose of vaccine
- visit 4: 24 months after the first dose of vaccine

COVID-19 vaccination

You will have received your second dose of vaccine around 3 weeks after your first vaccine dose, but the timing of vaccination may vary depending on vaccine availability and when your local centre contacted you for vaccination.

Blood sampling visits

At each visit, you will be asked to complete a short questionnaire and provide a blood sample.

Around 10 to 20 mls of blood (1 tablespoon) will be taken by a trained member of staff or a phlebotomist. For some participants, we will ask permission to take some more blood (15 to 30 ml, or 2 tablespoons) during some of the visits to test for cellular immunity.

For each visit, we will arrange the blood sampling to be done at a time and place that is convenient to you. This may be at your GP surgery, the local blood testing centre or at your home.

For each visit, the blood sample may be taken up to a week before or after the planned visit date.

If a blood sampling visit is missed, you can still continue to take part in the audit.

What will happen to your samples

Your blood samples will be sent to UKHSA, processed and stored with other samples until they are all tested together for SARS-CoV-2 antibodies. Any additional blood sample we collect will be sent to a specialist laboratory to test for cellular immunity. With your permission, we would like to store any remaining blood sample at UKHSA so that we may use for future test to understand virus infections and immunity. The samples will be stored anonymously and it will not be possible to link the sample back to you. You can choose what happens to any remaining samples on the consent form. You can still take part even if you ask us to have the blood sample destroyed after the tests are complete.

Taking part in this audit will be confidential

We will need to collect some personal information, including your name, date of birth, contact details and health information to help us understand the results of the tests that we perform and to contact you for future appointments. We will also need to access your electronic GP records in order to ascertain the dates when your vaccines have been given.

We will keep all the information securely as we do for all the tests we perform at UKHSA. We will write our reports in a way that no one can work out that you took part in the audit. All personal data will be stored in accordance with the General Data Protection Regulations (GDPR) and the Data Protection Act 2018.

What the benefits are to you

This audit will not benefit you directly, but your participation will support national immunisation policy to help better protect and improve health and well-being of the population. At the end of the evaluation, the overall results will be published in a UKHSA report.

What the disadvantages are

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 light headedness when the blood is drawn, and rarely, an infection at the site of the blood draw.

If you change your mind

If you no longer want to be involved, you can withdraw from the survey at any time and without giving a reason by contacting the UKHSA team (telephone (0208 495 3240) or email (Consensus@phe.gov.uk)).

What you should do now

If you would like to take part, please complete and sign the consent form. If you have any questions about the taking of the blood samples or any other questions about the audit, please do not hesitate to ask the team (telephone (0208 495 3240) or email (Consensus@phe.gov.uk)) and we will respond, Monday to Friday between 9 to 5pm.

Who has reviewed the audit

This work has been reviewed by UKHSA Research and Development team and the UKHSA Research Ethics and Governance of public health practice Group (UKHSA REGG).

What to do if you have any concerns

If you have any concerns, please talk to a member of the team. If you are still unhappy, you can contact the UKHSA Research and Development (R&D) Team (RandD.OFFICE@phe.gov.uk).

Funding

This audit is being supported by UKHSA and the Department of Health and Social Care

Extra costs incurred

If there are extra expenses are incurred in addition to the vaccination visits, these can be claimed back from UKHSA.

Appendix 3 : Information leaflet for booster programme

Information leaflet for participants

COVID-19 Vaccine Responses after booster dose

CONSENSUS (version 1, 11 August 2021)

We would like you to thank you for taking part in a national audit of the extended COVID-19 vaccine immunisation schedule that is recommended in the UK. Your data has been invaluable in evaluating the effectiveness of the different dosing schedules and influencing national immunisation policy.

In June the government announced a potential booster programme, which would likely begin in September 2021. If this programme is rolled out, we would like to alter the visit schedule, so we can monitor your immune response to the booster dose, should you be recommended to receive it. If you are given a booster dose we would like to test you:

- before or at the time you receive a booster dose
- approximately 4 to 6 weeks, 3, 6, 12 and 18 months after booster dose

So, the maximum number of blood tests over the whole study (including ones you have already had) could be 14, but this will be lower if we have recruited you after your first vaccine dose or you were vaccinated 3 weeks after dose 1 with Pfizer BioNTech. Before you decide whether to continue taking part, we would like you to re-read why we are doing this, and what the audit involves. Please ask us if there is anything that is not clear.

Why we are doing this audit

UK Health Security Agency (UKHSA) is undertaking this audit to assess the antibody levels offered by the extended 12 week schedule, that is currently recommended in the UK for COVID-19 vaccines and the antibody levels following a potential booster programme. We are looking for volunteers to provide blood samples from the time of their first vaccination until 24 months after their first dose of vaccine to measure the immunity provided by COVID-19 vaccine. There is currently limited data for this given the pace at which the vaccine has been rolled out, so this is really very important.

We will use the blood samples to measure antibodies provided by the COVID-19 vaccine against the novel coronavirus, SARS-CoV-2. For some participants, we may also ask to take some extra blood as some of the visits for additional cellular immunity tests (T cell and B cell immunity).

The results of the blood tests will provide important information about the level of immunity provided by the first dose until the second dose and potential booster doses and for up to 2

years since your first vaccine dose. We would like to include a range of people who are eligible for the COVID-19 vaccine, depending on their age, underlying medical problems, and whether they have had COVID-19 in the past

Why you have been asked to take part

You have been asked to take part because you are one of the first people to be offered the COVID-19 vaccine. We have limited data on the long-term level antibody levels provided by the vaccine, including booster doses, and the results of yours and other participants' blood tests will be used to inform public health guidance and recommendations on the need for future COVID-19 vaccinations

Donating the blood sample is voluntary - it is up to you to decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form.

What we want you to do

To monitor the booster programme, if you decide to take part, we will arrange the following visits with you:

- visit 1: Before or at the time of booster vaccine
- visit 2: 4 to 6 weeks after booster dose
- visit 3: 3 months after booster dose
- visit 4: 6 months after booster dose
- visit 5: 12 months after booster dose
- visit 6: 18 months after booster dose

COVID-19 vaccination

Depending on when you were recruited to the study, you should have had at least 1 COVID-19 vaccine already. The timing of your second and booster dose may vary depending on vaccine availability and when your local centre contacted you for vaccination.

Blood sampling visits

At each visit, you will be asked to complete a short questionnaire and provide a blood sample.

Around 10 to 20 mls of blood (about 1 tablespoon) will be taken by a trained member of staff or a phlebotomist. For some participants, we will ask permission to take some more blood (15 to 30 ml, or 1 to 2 tablespoons) during some of the visits to test for cellular immunity.

For each visit, we will arrange the blood sampling to be done at a time and place that is convenient to you. This may be at your GP surgery, the local blood testing centre or at your home.

For each visit, the blood sample may be taken up to a week before or after the planned visit date.

If you are unable to attend in person, we may send you a special blood sampling kit called a Tasso device. Tasso devices may also prove to be a good way of collecting blood at later visit time points. A Tasso device is a small round device which you place on your upper arm and press a push button to draw a very small amount of blood painlessly into the special tube provided. We will arrange to send the kits to you and have them returned to us by post or courier. We will include full instructions when we send you the kit. We will also be available to help you over the phone if needed

If a blood sampling visit is missed, you can still continue to take part.

What will happen to your samples

Your blood samples will be sent to UKHSA, processed and stored with other samples until they are all tested together for SARS-CoV-2 antibodies. Any additional blood sample we collect will be sent to a specialist laboratory to test for cellular immunity. With your permission, we would like to store any remaining blood sample at UKHSA so that we may use for future test to understand virus infections and immunity. The samples will be stored anonymously and it will not be possible to link the sample back to you. You can choose what happens to any remaining samples on the consent form. You can still take part even if you ask us to have the blood sample destroyed after the tests are complete.

Taking part in this audit will be confidential

We will need to collect some personal information, including your name, date of birth, contact details and health information to help us understand the results of the tests that we perform and to contact you for future appointments. We will also need to access your electronic GP records in order to ascertain the dates when your vaccines have been given.

We will keep all the information securely as we do for all the tests we perform at UKHSA. We will write our reports in a way that no one can work out that you took part in the audit. All personal data will be stored in accordance with the General Data Protection Regulations (GDPR) and the Data Protection Act 2018.

What the benefits are to you

This important audit will not benefit you directly, but your participation will support national immunisation policy to help better protect and improve health and well-being of the

population. At the end of the audit, the overall results will be published in a UKHSA report, and we can provide you with a copy if you wish.

What the disadvantages are

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 light headedness when the blood is drawn, and rarely, an infection at the site of the blood draw.

If you change your mind

If you no longer want to be involved, you can withdraw from the audit at any time and without giving a reason by contacting the UKHSA team (Monday-Friday 9am to 5pm, telephone: 0208 495 3240 or email: Consensus@phe.gov.uk.

What you should do now

If you would like to continue participating in the CONSENSUS study, please complete and sign the consent form. If you have any questions about the taking of the blood samples or any other questions about the audit, please do not hesitate to ask the team (telephone: 0208 495 3240 or email: Consensus@phe.gov.uk between Monday – Friday 9am to 5pm

Who has reviewed the audit

This work has been reviewed by UKHSA Research and Development team and the UKHSA Research Ethics and Governance of public health practice Group (UKHSA REGG).

What to do if you have any concerns

If you have any concerns, please talk to a member of the team. If you are still unhappy, you can contact the UKHSA Research and Development (R&D) Team (RandD.OFFICE@phe.gov.uk).

Funding

This audit is being supported by UKHSA and the Department of Health and Social Care

Extra costs incurred

If there are extra expenses are incurred in addition to the vaccination visits, these can be claimed back from UKHSA.

Appendix 4 : Consent forms

CONSENSUS Participant study number_____

Consent form for participants (version 6, dated 30 March 2021)

COVID-19 vaccine responses after extended immunisation schedules

		Initial
1	I have read the Information Leaflet for Participants on the "COVID-19 Vaccine Responses after extended immunisation schedules" (version 1.2, dated 18 January 2021)	
2	I have been given sufficient time to consider making this decision and have had all my questions answered satisfactorily	
3	I agree to take part in the audit and to complete a short questionnaire and provide blood sample at each visit before and after receiving my COVID-19 vaccine	
4	I understand that my personal data will be stored in accordance with the Data Protection Act 2018 and the GDPR	
5	I understand that my samples will be tested for immunity against the novel coronavirus, SARS-CoV-2, including antibodies against the virus	
6	I have been informed that I can withdraw at any time without giving a reason.	
7	I understand that my electronic GP records may need to be accessed (EMIS) to obtain relevant medical history.	
	The following are optional. If you choose to withhold consent for either or both of them, you can still take part in the audit	
8	I am happy for UKHSA to use any remaining blood sample anonymously to better understand immunity against viruses	
9	I would like to receive a copy of the audit report	

Name of participant: _____Signature: _____

Contact phone: _____ Email: _____

Date: _____Signature of professional_____

Consent form for participants

COVID-19 vaccine responses after the standard dose immunisation schedules

		Initial
1	I have read the Information Leaflet for Participants on the “COVID-19 Vaccine Responses after the standard immunisation schedule” (Version 1.2, Dated 18 January 2021)	
2	I have been given sufficient time to consider making this decision and have had all my questions answered satisfactorily	
3	I agree to take part in the audit and to complete a short questionnaire and provide blood sample at each visit before and after receiving my COVID-19 vaccine	
4	I understand that my personal data will be stored in accordance with the Data Protection Act 2018 and the GDPR	
5	I understand that my samples will be tested for antibody levels and/or cellular against the novel coronavirus, SARS-CoV-2, including antibodies against the virus	
6	I have been informed that I can withdraw at any time without giving a reason.	
	The following are optional. If you choose to withhold consent for any of them, you can still take part in the audit.	
7	I understand that my electronic GP records may need to be accessed (EMIS) to obtain relevant medical history.	
8	I am happy for UKHSA to use any remaining blood sample anonymously to better understand immunity against viruses	
9	I would like to receive a copy of the audit report	

Name of Participant: _____Signature: _____

Date: _____ Signature of Professional _____

CONSENSUS Participant study number_____

Consent form for participants (version 1, dated 11 August 2021)

COVID-19 vaccine responses after booster vaccine

		Initial
1	I have read the Information Leaflet for Participants on the "COVID-19 Vaccine Responses after booster dose" (Version 1, Dated 11 August 2021)	
2	I have been given sufficient time to consider making this decision and have had all my questions answered satisfactorily	
3	I agree to take part in the audit and to complete a short questionnaire and provide blood sample at each visit before and after receiving my COVID-19 booster vaccine	
4	I understand that my personal data will be stored in accordance with the Data Protection Act 2018 and the GDPR	
5	I understand that my samples will be tested for immunity against the novel coronavirus, SARS-CoV-2, including antibodies against the virus	
6	I have been informed that I can withdraw at any time without giving a reason.	
7	I understand that my electronic GP records may need to be accessed (EMIS) to obtain relevant medical history.	

The following are optional. If you choose to withhold consent for either or both of them, you can still take part in the audit

8	I am happy for UKHSA to use any remaining blood sample anonymously to better understand immunity against viruses	
9	I would like to receive a copy of the audit report	

Name of participant: _____Signature: _____

Contact phone: _____ Email: _____

Date: _____ Signature of professional_____

Appendix 5 : Participant reference number

Blood sampling should ideally take place at the schedule visit week but may be taken up to one week before or after the next due appointment

Date of appointment	Questionnaire completed?	Blood sample taken?	Date of next appointment	Signature of Audit team
	Yes / No	Yes / No		
	Yes / No	Yes / No		
	Yes / No	Yes / No		
	Yes / No	Yes / No		
	Yes / No	Yes / No		
	Yes / No	Yes / No		

Notes/comments:

Appendix 6 : Questionnaire for participants

Participant questionnaire (at time of recruitment)

Participant ID:_____ DOB _____ Practice name:_____

Telephone no:_____ Email:_____ Preferred contact: T / E

Which one of the following groups do you belong to?

White ☐ English / Welsh / Scottish / Northern Irish / British ☐ Irish ☐ Gypsy or Irish Traveller ☐ Any other White background Mixed / multiple ethnic groups ☐ White and Black Caribbean ☐ White and Black African ☐ White and Asian ☐ Any other mixed / multiple ethnic background Black / African / Caribbean / Black British ☐ African ☐ Caribbean ☐ Any other Black / African / Caribbean	Asian / Asian British ☐ Indian ☐Pakistani ☐Bangladeshi ☐ Chinese ☐Any other Asian background Other ethnic group ☐ Arab ☐ Any other ethnic group (state below)*:* ☐ Prefer not to answer

Have you got any current medical conditions? Yes / No

If yes, please state:

If you are currently working, please state your occupation

Frontline HCW (Hospital) ☐ Frontline HCW (Community) ☐ Social Care Worker ☐

Care home worker ☐ Retired ☐ Other (please specify) _____

Household Composition

a. Number of children under 18 years in your household: _____
b. Number of adults (including yourself) aged 18 to 69 years in your household_____
c. Number of older adults aged 70 years and over (including yourself) over in your household:_____

History of COVID-19 related illness or symptoms

Have you had any COVID-19 related symptoms in the past year?

- Yes, I had symptoms but I was not tested
- Yes, I had symptoms but my test(s) were all negative
- Yes, I had symptoms and I had at least one positive test
- Yes, I had symptoms, had a test, but it failed
- No
- I am not sure

If yes, when did your COVID-19 related symptoms start?

Approximate dates are fine. If you have had symptoms more than once, record the first date. Please use the calendar or enter in DD/MM/YYYY, example 21/01/2020.

If yes, how long were you ill for? days

If yes, were you admitted to hospital? Y /N

If you had a positive COVID-19 result, what date was the sample that was taken which had a positive COVID-19 result?

_____/_____/_____

Has anyone else in your household tested positive for COVID-19?

Yes / No – if yes, approximate number of people

Have you had any recent (within last 14 days) exposure to someone with confirmed COVID-19?

Yes / No – if yes, date of exposure

History of COVID-19 vaccination (if applicable)

First dose: date _____ Vaccine type: _____

Second dose: date _____ Vaccine type: _____

If received either vaccine please complete next page

Thank you for taking the time to complete the questionnaire.

Did you develop any symptoms after your first vaccine? Y / N

For each of the symptoms listed below, please use the scale below to grade any symptoms

□ 0 No symptoms
□ 1 Mild – easily tolerated with no limitation on normal activity
□ 2 Moderate – some limitation of daily activity
□ 3 Severe – unable to perform normal daily activity
□ 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)					Duration of symptoms (number of days)
Fever	0	1	2	3	4	
Chills	0	1	2	3	4	
Headache	0	1	2	3	4	
Generally unwell	0	1	2	3	4	
Tiredness	0	1	2	3	4	
Joint pain / aches	0	1	2	3	4	
Nausea / vomiting	0	1	2	3	4	
Reaction at injection site						
Pain	0	1	2	3	4	
Tenderness	0	1	2	3	4	

Itching	0 1 2 3 4	
Redness / Warmth	0 1 2 3 4	
Other		

Did you develop any symptoms after your second vaccine? Y / N

For each of the symptoms listed below, please use the scale below to grade any symptoms

□ 0 No symptoms
□ 1 Mild – easily tolerated with no limitation on normal activity
□ 2 Moderate – some limitation of daily activity
□ 3 Severe – unable to perform normal daily activity
□ 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)	Duration of symptoms (number of days)
Fever	0 1 2 3 4	
Chills	0 1 2 3 4	
Headache	0 1 2 3 4	
Generally unwell	0 1 2 3 4	
Tiredness	0 1 2 3 4	
Joint pain / aches	0 1 2 3 4	
Nausea / vomiting	0 1 2 3 4	
Reaction at injection site		
Pain	0 1 2 3 4	
Tenderness	0 1 2 3 4	
Itching	0 1 2 3 4	
Redness / warmth	0 1 2 3 4	
Other		

Participant questionnaire (at each follow up visit)

This questionnaire will be developed online using the UKHSA Snap Survey tool

Participant ID:

Age:

Gender: [] Male [] Female [] Prefer not to answer

History of COVID-19 related illness or symptoms

Have you had any COVID-19 related symptoms since your last visit?

- Yes, I had symptoms but I was not tested
- Yes, I had symptoms but my test(s) were all negative
- Yes, I had symptoms and I had at least one positive test
- Yes, I had symptoms, had a test, but it failed
- No
- I am not sure

If yes, when did your COVID-19 related symptoms start?

Approximate dates are fine. If you have had symptoms more than once, record the first date. Please use the calendar or enter in DD/MM/YYYY, example 21/01/2020.

_____ /_____ /_____

If yes, how long were you ill for? _____ days

If yes, were you admitted to hospital? Y /N

If you had a positive COVID-19 result, what date was the sample that was taken which had a positive COVID-19 result?

_____ /_____ /_____

Has anyone else in your household tested positive for COVID-19?

- Yes / No – if yes, approximate number of people

Post Vaccination Symptoms (to be completed for first visit after dose 1 and 2)

Did you develop any symptoms after your first vaccine? Y / N

For each of the symptoms listed below, please use the scale below to grade any symptoms

□ 0 No symptoms
□ 1 Mild – easily tolerated with no limitation on normal activity
□ 2 Moderate – some limitation of daily activity
□ 3 Severe – unable to perform normal daily activity
□ 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)	Duration of symptoms (number of days)
Fever	0 1 2 3 4	
Chills	0 1 2 3 4	
Headache	0 1 2 3 4	
Generally unwell	0 1 2 3 4	
Tiredness	0 1 2 3 4	
Joint pain / aches	0 1 2 3 4	
Nausea / vomiting	0 1 2 3 4	
Reaction at injection site		
Pain	0 1 2 3 4	
Tenderness	0 1 2 3 4	
Itching	0 1 2 3 4	
Redness / warmth	0 1 2 3 4	
Other		

Did you develop any symptoms after your second vaccine? Y / N

For each of the symptoms listed below, please use the scale below to grade any symptoms

□ 0 No symptoms
□ 1 Mild – easily tolerated with no limitation on normal activity
□ 2 Moderate – some limitation of daily activity
□ 3 Severe – unable to perform normal daily activity
□ 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)					Duration of symptoms (number of days)
Fever	0	1	2	3	4	
Chills	0	1	2	3	4	
Headache	0	1	2	3	4	
Generally unwell	0	1	2	3	4	
Tiredness	0	1	2	3	4	
Joint pain /aches	0	1	2	3	4	
Nausea /Vomiting	0	1	2	3	4	
Reaction at injection site						
Pain	0	1	2	3	4	
Tenderness	0	1	2	3	4	
Itching	0	1	2	3	4	
Redness / Warmth	0	1	2	3	4	
Other						

Week 15 participant questionnaire

Date _____

Participant ID: _____ Name:_____

DOB: _____

Please can you confirm your preference for contact: Email/address/both?

Email:

Address:

Which vaccine/s were you given?

First vaccine:_____ Date: _____ Batch no: _____

Second vaccine:_____ Date: _____ Batch no: _____

Verified on card: Y N n/a

If you have not had your second dose, do you have an appointment booked?

Yes Date _____

Reason for delay:_____

No

Have there been any changes to your household since your last visit? Yes /No

If yes, please provide further details

_____

History of COVID-19 related illness or symptoms

Have you had any COVID-19 related symptoms since your last visit?

- Yes, I had symptoms but I was not tested
- Yes, I had symptoms but my test(s) were all negative
- Yes, I had symptoms and I had at least one positive test
- Yes, I had symptoms, had a test, but it failed
- No
- I am not sure

Vaccine symptom gathering at week 15 visit

In the following two pages we are clarifying symptoms after both the first and second vaccine so please accept our apologies if you have given this data previously – we need to ensure accuracy before reporting.

Symptoms after the first vaccine dose

Please circle Yes or No:

Did you develop any symptoms after your first vaccine? Yes / No

If you did get symptoms after the first vaccine dose – which did you get?

Fever: Yes/No

Chills: Yes/No

Headache: Yes/No

Generally unwell: Yes/No

Tiredness: Yes/No

Joint pain/athralgia: Yes/No

Nausea/vomiting: Yes/No

Reaction at the injection site: Yes/No

For each of the symptoms listed below, please use the scale below to grade any symptoms

 0 No symptoms

 1 Mild – easily tolerated with no limitation on normal activity

 2 Moderate – some limitation of daily activity

 3 Severe – unable to perform normal daily activity

 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)	Duration of symptoms (number of days)
Fever	0 1 2 3 4	
Chills	0 1 2 3 4	

Headache	0	1	2	3	4	
Generally unwell	0	1	2	3	4	
Tiredness	0	1	2	3	4	
Joint pain / aches	0	1	2	3	4	
Nausea / vomiting	0	1	2	3	4	
Reaction at injection site						
Pain	0	1	2	3	4	
Tenderness	0	1	2	3	4	
Itching	0	1	2	3	4	
Redness / warmth	0	1	2	3	4	
Other						

Symptoms after the second vaccine dose

Please circle Yes or No:

Did you develop any symptoms after your second vaccine? Yes / No

If you did get symptoms after the first vaccine dose – which did you get?

Fever: Yes/No

Chills: Yes/No

Headache: Yes/No

Generally unwell: Yes/No

Tiredness: Yes/No

Joint pain/athralgia: Yes/No

Nausea/vomiting: Yes/No

Reaction at the injection site: Yes/No

Other symptoms: Yes/No

For each of the symptoms listed below, please use the scale below to grade any symptoms

 0 No symptoms

 1 Mild – easily tolerated with no limitation on normal activity

 2 Moderate – some limitation of daily activity

 3 Severe – unable to perform normal daily activity

 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)					Duration of symptoms (number of days)
Fever	0	1	2	3	4	
Chills	0	1	2	3	4	
Headache	0	1	2	3	4	
Generally unwell	0	1	2	3	4	
Tiredness	0	1	2	3	4	
Joint pain / aches	0	1	2	3	4	
Nausea / vomiting	0	1	2	3	4	
Reaction at injection site						
Pain	0	1	2	3	4	
Tenderness	0	1	2	3	4	
Itching	0	1	2	3	4	
Redness / warmth	0	1	2	3	4	
Other						

Appendix 7 : Booster follow-up visit questionnaire

Participant questionnaire (at each follow up visit)

This questionnaire will be developed online using the UKHSA Snap Survey tool

Participant ID:

Age:

Gender: [] Male [] Female [] Prefer not to answer

Which booster vaccine were you given?

Booster dose type:_____ Date: _____ Batch no: _____

Verified on card: Y N n/a

Have you received a flu vaccination this year? Y / N

Date: _____ Type (if known): _____

History of COVID-19 related illness or symptoms

Have you had any COVID-19 related symptoms since your last visit?

- Yes, I had symptoms but I was not tested
- Yes, I had symptoms but my test(s) were all negative
- Yes, I had symptoms and I had at least one positive test
- Yes, I had symptoms, had a test, but it failed
- No
- I am not sure

If yes, when did your COVID-19 related symptoms start?

Approximate dates are fine. If you have had symptoms more than once, record the first date. Please use the calendar or enter in DD/MM/YYYY, example 21/01/2020.

__ __/__ __/ __ __ __ __

If yes, how long were you ill for? _____ days

If yes, were you admitted to hospital? Y /N

If you had a positive COVID-19 result, what date was the sample that was taken which had a positive COVID-19 result?

_____ /_____ /_____

Has anyone else in your household tested positive for COVID-19?

Yes / No – if yes, approximate number of people

Post booster vaccination symptoms (to be completed 4 to 6 weeks after booster vaccine)

Did you develop any symptoms after your booster vaccine? Y / N

For each of the symptoms listed below, please use the scale below to grade any symptoms

□ 0 No symptoms
□ 1 Mild – easily tolerated with no limitation on normal activity
□ 2 Moderate – some limitation of daily activity
□ 3 Severe – unable to perform normal daily activity
□ 4 Emergency department or hospital admission required

Symptoms	Scale (0-4), please circle: 0(no symptoms) 4(symptoms)	Duration of symptoms (number of days)
Fever	0 1 2 3 4	
Chills	0 1 2 3 4	
Headache	0 1 2 3 4	
Generally unwell	0 1 2 3 4	
Tiredness	0 1 2 3 4	
Joint pain / aches	0 1 2 3 4	
Nausea / vomiting	0 1 2 3 4	
Reaction at injection site		
Pain	0 1 2 3 4	
Tenderness	0 1 2 3 4	
Itching	0 1 2 3 4	

Redness / warmth	0 1 2 3 4	
Other		

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation heath secure.

UKHSA is an executive agency, sponsored by the Department of Health and Social Care.

Published: March 2022
Publishing reference: GOV-11439

UKHSA supports the Sustainable Development Goals