PARTICIPANT INFORMATION SHEET:

Comparing COVID-19 Vaccine Schedule Combinations (Com-COV)

We are recruiting people 50 years of age and over to a study of 'mixed' schedules of different COVID-19 vaccines. Please express an interest if you want to help!

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Participation could really make a difference during a public health emergency.

Thank you for reading this, your help, whatever your final decision, is very much valued. We would like to invite you to take part in our Comparing COVID-19 Vaccine Schedule Combinations study (Com-COV). Before you make any decision, it is important you take the time to understand why we are doing this research and what it would involve. Please read the following information carefully and consider discussing it with friends, relatives or others as you wish.

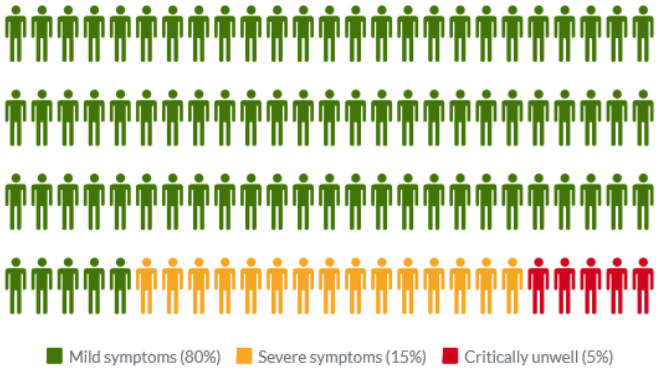
What is the purpose of this research trial?

There are now a number of vaccines that have been approved to prevent COVID-19 in the UK. These use two-doses, a 'prime' first dose, followed by a 'boost' second dose some weeks later. The purpose of this trial is to see how well people's immune systems respond when they are primed with one type of vaccine, then boosted with another and to see how good the response is when the second dose is separated from the first dose by different periods of time. We will also be looking at how common vaccine reactions, such as fever, are after such 'mixed' schedules. This is important, as being able to combine different vaccines in this way, creates a more flexible immunisation programme, potentially allowing more people to be immunised more quickly. It will also give us useful information about extending the gap between prime and boost. We will be enrolling men and women aged 50 years and over from all ethnicities; and would particularly welcome participants from the Black and Minority Ethnic (BAME) community.

What are the vaccines against?

These vaccines are against the new coronavirus SARS-CoV2 that causes the disease COVID-19.

Common symptoms of COVID-19 include fever, tiredness, dry cough, and changes to taste and smell. Whilst about 80% of infected people have no or mild symptoms and will recover from the infection without needing special treatment, approximately 10-15% of cases (2-3 in 20) progress to develop severe symptoms, and about 5% (1 in 20) become critically ill.



There are some treatments that have been shown to be effective in reducing the severity of disease and the risk of death; but at present there is no cure. Older people and those with underlying medical conditions are more likely to develop serious illness. It has also been seen that people of some ethnic groups (Black and Asian) might be at a greater risk of severe illness. More than 1.4 million people globally have died from COVID-19 so far. Some people also have symptoms that last a long time after they have recovered (commonly referred to as "long-COVID"). This is why effective vaccines are so important.

Summary of the trial

We are studying combinations of two different vaccines, and there will be 820 participants. As more new SARS-CoV-2 vaccines become available, more vaccines may be included in the trial and so the total number of participants may increase.

- Participants will be allocated, at random, (rather like a flip of a coin) to receive one dose of one approved vaccine and a second dose of either the same approved vaccine, or a dose of a different approved vaccine. Participants will also be allocated at random to the timing of receiving these doses – some will get a boost dose four weeks after the first dose (prime) and some will get a boost at twelve weeks.
- Between 5 and 10 routine blood tests will be taken over the course of a year to look at the immune responses to the vaccine depending on the group you are in. You may also be asked for a nasal fluid sample and an (optional) saliva sample at each visit. You might also be asked to attend for a repeat blood test if there were any safety concerns. If you were to test positive for the virus causing COVID-19 we may ask you to attend for an extra visit.
- Participants will need to complete an online diary for up to 28 days following each of the two vaccinations
- The trial will take one year to complete per participant (from the time the first dose of vaccine is given)
- We would not be offering diagnostic COVID-19 testing as part of this trial, but it is important that participants in this trial access COVID-19 testing outside of the trial following normal government guidance.
- If you receive the two doses of COVID-19 vaccines in this trial, you would not know which two vaccines you had received until the end of the trial. Unless specifically

advised by us, you would not be eligible to receive any further vaccine doses via the government vaccination scheme.

What vaccines are being used in this trial?

The two vaccines in this trial are ChadOx1 nCoV-19 (also known as AZD1222, developed in Oxford and manufactured by AstraZeneca) and BNT162b2 (manufactured by Pfizer BioNTech), and the vaccine schedules received in the study are shown below.

Prime	Boost (28 or 84 days later)
ChadOx1 nCoV-19 (AstraZeneca/Oxford)	ChadOx1 nCoV-19 (AstraZeneca/Oxford)
ChadOx1 nCoV-19 (AstraZeneca/Oxford)	BNT162b2 (Pfizer/BioNTech)
BNT162b2 (Pfizer/BioNTech)	BNT162b2 (Pfizer/BioNTech)
BNT162b2 (Pfizer/BioNTech)	ChadOx1 nCoV-19 (AstraZeneca/Oxford)

ChAdOx nCoV-19 (AstraZeneca/Oxford)

This is the vaccine that is commonly known as the "Oxford vaccine". It has been tested in more than 20,000 people worldwide as part of the COVID-19 vaccine trials. It has been found to be both safe, and effective in preventing COVID-19.

ChAdOx1 nCoV-19 is made from a virus (ChAdOx1), which is a weakened version of a common cold virus (adenovirus). This has been genetically changed so that it is impossible for it to grow in humans. Added to this virus are genes that make proteins from the COVID-19 virus (SARS-CoV-2) called Spike glycoprotein (S), which play an essential role in SARS-CoV-2 infection. By vaccinating with ChAdOx1 nCoV-19, the body recognises and develops an immune response to the Spike protein that helps stop SARS-CoV-2infections.

BNT162b2 (Pfizer/BioNTech)

This is the vaccine commonly known as 'The Pfizer vaccine.' This is a messenger RNA (mRNA) vaccine. This vaccine uses a small amount of the genetic coding material (mRNA) of the SARS-CoV-2 spike (S) protein packaged inside very small fatty particles (lipid nanoparticles). When these are injected into your body, your cells take up these fatty particles, and then start producing the SARS-CoV-2 spike protein. Your immune system then "sees" these spike proteins, and makes a protective immune reaction against them. The original mRNA that has been taken into your cells is broken down within a few days, and cannot be incorporated into your own genetic code.

This vaccine has been tested in more than 40,000 people worldwide and has been shown to be both safe, and effective.

Neither vaccine contains the SARS-CoV-2 coronavirus and therefore cannot give you COVID-19. The potential side effects of these vaccines are discussed in more detail in the section 'What are the risks of taking part in this trial'.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep (or be sent it electronically) and will be asked to sign a consent form. You are free to withdraw at any time and without giving a reason, but you may be asked to come for an extra visit for a follow up appointment for safety reasons.

Am I suitable to take part?

Adults that are aged 50 and over are able to take part. In order to be enrolled in the trial:

- You must be willing to tell the trial staff about your medical history, and you may be asked to allow the trial staff to check this with your General Practitioner (GP). Bear in mind that we would also notify your GP if you joined the trial (even if we did we not need to check your medical history with them in advance).
- If you are able to become pregnant you must be willing to practice continuous effective contraception during the trial and have negative pregnancy tests on the days of vaccination
- You must agree not to donate blood during the trial

You cannot take part in this trial if you:

- Have already received one or more doses of the NHS COVID-19 vaccine
- Are already taking part in any trial looking to prevent COVID-19 through vaccines or medications
- Have any vaccine in the 30 days before or after this trial vaccine. The exceptions to this are the seasonal influenza vaccine and the pneumococcal vaccine (known as Pneumovax, which is routinely given to over 65-year olds). If you are offered these by your GP or your place of work, we ask that you have these at least 7 days before or after you receive either of the two trial vaccine doses.
- Have previously received certain vaccines (such as other adenovirus-based vaccines) that might impact on understanding your results. If you are not sure about this, please contact us to discuss.
- Have received a transfusion of any blood products, or immunoglobulins (antibodies) in the 3 months before having the trial vaccine
- Have immunosuppression or immunodeficiency – this includes being on medications that reduce the immune system such as methotrexate and steroid tablets
- Have ever had a severe allergic reaction (anaphylaxis)
- Have an allergy to any of the component of the COVID vaccines used in this study, including polyethylene glycol/macrogol (PEG). PEGs are a group of known allergens commonly found in medicines, many household products and cosmetics, and are contained in the BNT162b2 (Pfizer/BioNTech) vaccine. Known allergy to PEG is very rare.
- Are pregnant, breastfeeding or intend to become pregnant during the trial

- Have a current diagnosis of, or are having treatment for, cancer. Exceptions to this are certain skin cancers and pre-cancer of the cervix.
- Have a bleeding disorder
- Continuously take medicines that reduce your blood clotting, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban)
- Have current alcohol or drug dependency
- Have severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder or neurological illness
- Have a history of confirmed COVID-19 by a validated test or have previously had a blood test that shows that you have had contact with the COVID-19 virus (antibody test)

To assess if you are eligible to be involved in the trial you can complete the online eligibility questionnaire as described below.

What will happen if I decide to take part?

Online questionnaire – *5-20 minutes*

If you decide you would like to participate in this trial there is a two-part online questionnaire to check initial eligibility.

Part-One

The first part broadly checks whether you can or cannot take part in the trial. The information you provide will not be stored unless you progress to part two.

Part-Two

If you are found to be eligible on completing the first part, you will be asked to give your consent to:

- Provide us with details of your medical history and allow us to store this information. Some participants will be advised they are unable to take part on the basis of this additional information
- Have a researcher contact you by phone to clarify the medical information given (if needed)
- Provide details of your registered GP, and consent for the trial team to contact them if needed
- Provide us with information about yourself such as your date of birth and address

If you do not consent to these things, then you would not be able to join the trial. If you consent and the second part of the questionnaire does not identify any obvious reason why

you should not participate, we will review the information you provide, and a trial doctor or nurse may telephone you to go through this in more detail if required.

If, after this process, you are eligible to join the trial, you will be invited to an in-person screening and vaccination visit.

IMPORTANT: If you develop a fever or cough, or loss of sense of smell or taste, or become unwell then you must contact the study team on com-cov@sgul.ac.uk for advice before attending any visit.

Please note that it may not be possible to enrol everybody that wishes to take part in the trial, and passing through the screening process does not guarantee participation in the trial. In the case that you are not enrolled in the trial, your data would not be stored beyond the end of the trial.

What should I do if I am offered the NHS vaccination before I am called for the first study visit?

It is up to you decide but you are free to accept the offer. You could wait to join the study and we will keep you informed of the likely date you will be called. There is no guarantee you will be enrolled. If you accept the NHS vaccination you will no longer be eligible to join the study

Also, there may be a period of a few months between you completing the screening and attending the first 'in person' trial visit. If this period exceeded 120 days (four months), we would ask you to complete the online screening check again.

Enrolment on the Study

Screening and vaccination visit - *1.5 hours (review of medical history, vital signs, blood test, receive vaccine, up to 30 minute observation in clinic after the vaccine)*

Screening component

If you qualify to be in the trial, we will ask you to attend on the vaccination day (Day 0). We will outline the nature of the trial either through a video presentation or in person, and this will explain what to expect by taking part, the risks involved and what side-effects you might expect to experience. There will be an opportunity to ask any questions you may have about the trial, and if you decide to take part we will ask you to sign a consent form.

If you sign the consent form a member of the medical team would check details of your medical history, and may perform a physical examination; which could involve listening to your heart and lungs with a stethoscope, examining your abdomen as well as feeling for lymph nodes around your neck and in your armpits. We will measure and record your:

- Height

- Weight
- Temperature
- Blood pressure
- Pulse rate
- Respiratory rate
- Non-invasive blood oxygen level (saturations)

Blood samples will be taken just before vaccination to check later for:

- Whether you have previously been infected with the COVID-19 virus (antibody test). Please note:
    - We would not give you the result of this test until the end of the trial and would only give it to you if you wished to receive it at this point.
    - If you do decide to receive the results of your antibody test at the end of the trial you should bear in mind that, like all medical tests, it is not 100% accurate. The results cannot be used to provide certainty of prior infection nor of protection from future infection.
    - Before asking for your results, you should consider whether they would have any effect on any private insurance you may have.
- Whether you are anaemic or have any other blood, kidney or liver abnormalities. Sometimes these blood tests need to be repeated, and we would ask you to come for an extra visit to have these taken. If, once available, the results indicate that it would not be safe to carry on in the trial we would let you know this. Additionally, regardless of whether you continue in the trial, we may ask for you permission to contact your GP or a specialist so that any further required treatment or investigation can be organised.

We would also (in some participants) ask to take a nasal fluid sample which are is to look at immune responses in the lining of the airways. This is not a test which would have clinically interpretable results; thus you would not be given these results. This test would be repeated at all subsequent visits, from the first visit that you had this test done.

Vaccination

Once your eligibility and consent are re-confirmed, you will be randomly allocated to receive one of the various vaccine combinations. You will not be told which specific vaccines you are going to receive, or in what order. You will only be told this at the end of the trial. The only exception to this would be if you were to become ill and it was felt to be medically necessary for you to know which vaccines you had received.

We will give you an injection with the vaccine into your arm. We will need to keep an eye on you for 15 – 30 minutes after the vaccine has been administered.

<u>Follow-up after vaccination</u>

Electronic Symptom Diary "e-diary" – *Completed at home*

We will give you a thermometer, tape measure and an "e-diary" account to record all your symptoms, your temperature and your vaccination site every day for 7 days after this first vaccination and the later booster.

After these 7 days, and for the next 3 weeks, we will ask you to record if you feel unwell or if you take any new medications. The research staff will monitor the e-diary and may telephone you to ask for more information.

You will also be asked to record in the diary any medical conditions for which you see a doctor/dentist until three months after your second (boost) vaccine, and any serious medical illnesses or hospital visits you may have over the course of the trial.

Follow-up visits – 30 minutes (vital signs, blood tests, nasal fluid test and saliva test (for some participants) and check for side effects or new health problems)

Following vaccination, we will ask you to attend a series of short follow-up visits to ensure everything is fine, to check your symptoms and to have blood tests done as well as nasal fluid tests and optional saliva tests for some participants.

Note: due to the high number of planned volunteers in this trial, visits may take longer than the estimates given here

During the course of the trial you may be asked to attend for an extra visit, for example, if a blood test needs to be repeated.

In the unlikely event of you having a problem with your arm where the vaccination was given, we might ask to photograph your arm. Consent for this is included when you are enrolled to the study. You would not be identifiable in these photographs, as only the vaccination site and your unique trial number would be visible. These photographs could be shown to other professional staff, used for educational purposes, or included in a scientific publication.

How many visits will I have to attend?

The number of visits you attend will be the same regardless which vaccines you are randomly assigned to. However, each vaccine combination will also have an 'immunology' cohort who will have some extra visits and blood tests and nasal fluid and optional saliva tests; enrolment to this cohort is limited to 100 participants. The purpose of this will be to better understand the response of the immune system to the vaccine. If you would prefer not to be in the immunology cohort, then this is not a problem. Participants who are not in the 'immunology' cohort will be in the 'general' cohort and will be randomly assigned either to receive their second vaccine 28 days or 84 days after the first vaccine. If you are in the 28 day group of the general cohort, you will have 5 visits, whilst if you are in the 84 day group of the general cohort you will have 6 visits and may also be asked for nasal fluid and saliva.

General cohort 28-day boost (Regular frequency sampling cohort)

The table below represents the visit schedule for participants in the general cohort, boosted at 28 days:

Visit schedule for participants in the general cohort, boosted at 28 days					
Trial timeline	**Day 0**	**Day 28**	**Day 56**	**Day 182**	**Day 364**
Vaccinations	Prime (1^{st})	Boost (2^{nd})			
Blood tests	Yes	Yes	Yes	Yes	Yes
Nasal fluid test &/or Saliva test	No	No	No	No	No

General cohort 84-day boost (Regular frequency sampling cohort)

The table below represents the visit schedule for participants in the general cohort, boosted at 84 days.

Visit schedule for participants in the general cohort, boosted at 84 days						
Trial timeline	**Day 0**	**Day 56**	**Day 84**	**Day 112**	**Day 182**	**Day 364**
Vaccinations	Prime (1^{st})		Boost (2^{nd})			
Blood tests	Yes	Yes	Yes	Yes	Yes	Yes
Nasal fluid test	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)
Saliva test (optional)	-	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)	Yes (some participants only)

Immunology cohort (More frequent sampling cohort)

The table below represents the visit schedule for participants in the immunology cohort:

Visit schedule for participants in the immunology cohort										
Trial timeline	**Day 0**	**Day 7**	**Day 14**	**Day 28**	**Day 35**	**Day 42**	**Day 56**	**Day 112 (optional)**	**Day 182**	**Day 364**
Vaccinations	Prime (1^{st})			Boost (2^{nd})						
Blood tests	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Nasal fluid test	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Saliva test (optional)	-	-	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Should you be unable to attend a scheduled visit (for example because you are self-isolating or quarantining), then a researcher might do this visit over the phone with you instead (as long as it was on the correct schedule).

Also, regardless of which group or cohort you are in, if you were to test positive for COVID-19 outside of the trial, we would ask you to inform us of this and we would then ask you to attend for a medical check and to take further blood tests and a nose and throat swab. We would also ask you for a nasal fluid sample and an optional saliva sample if this was something you provided at your other routine visits. We would only ask you to come in for this visit if you were able to attend using your own transport; and didn't need anyone to come with you. We would ask you to fill in another electronic diary for at least a week after you were diagnosed with COVID-19. You would need to follow current government guidance for people with positive COVID-19 tests.

What things should I consider before taking part in this study?

If you are of female sex and able to have children, you must be willing to practise continuous effective contraception during the trial; methods of effective contraception are listed in the eligibility questionnaire.

Blood Donation

Under current UK regulations, participants will not be able to donate blood during the course of the trial.

Private Insurance

If you have private medical or travel insurance you are advised to contact your insurance company before participating in this trial, as involvement may affect the cover provided.

Are there things I will be asked to avoid doing during the trial?

You should not donate blood during the trial or take part in other studies that involve blood sampling or the administration of drugs or vaccines, including trials testing other preventive interventions for COVID-19. Once you have received two vaccines in this study, you will also not be able to receive any routine immunisation against COVID-19 that becomes available during your participation – more information about this is included below.

If during the trial you require any other vaccinations for health, travel, or occupational reasons, you should inform the trial team beforehand. We will discuss with you the most appropriate time to receive them.

What are the risks of taking part in this trial?

The risks and side effects of the proposed vaccinations and trial procedures are detailed here:

Blood samples

Drawing blood may cause slight pain and occasionally bruising at the site where the needle enters. Some people feel light-headed or even faint when having blood taken. During the course of the trial we will need to take between 20ml and 74ml of blood at a single visit. The total amount we will take over the period of the trial will be (approximately) 271ml if you are in the general cohort with a booster at 28 days, or (approximately) 321ml if you are in the general cohort with a booster at 84 days or (approximately) 528ml if you are in the immunology cohort. An additional 57-77ml would be taken at the COVID-19 pathway visit if you were to develop confirmed COVID-19 during the study. If repeat bloods are requested for safety reasons at a visit this will be up to 7ml. These amounts over the course of the year, should be below the limit of 470mL every 3 – 4 months for blood donations to the National Blood Transfusion Service.

If abnormal results or undiagnosed conditions are found during the course of the trial these will be discussed with you and, if you agree, your GP (or a hospital specialist, if more appropriate) will be informed. Any newly diagnosed conditions will be looked after within the NHS. Participants will not be informed of the results of their levels of post-vaccine immunity against the COVID-19 virus as these are not clinically validated tests.

Nasal fluid samples

This will involve insertion of a small bit of soft synthetic material about 2cm into your nostril and leaving it in there, pressed up against the inside of your nose for about one minute. This can cause some eye-watering, but should not cause any damage to your nostrils. Some people might have more sensitive nostril linings and this might rarely cause a small amount of bleeding.

Saliva samples (optional)

We aim to collect 1-1.5mls saliva using a funnel and collection tube. Participants may find the saliva collection process unsavoury as it is involves drooling and spitting into a collection device.

If you are having nasal fluid samples taken, we may also ask for optional saliva samples at routine visits from 28 days after your first vaccine dose. We would ask participants who are giving saliva samples, not to eat, drink, smoke, chew gum, brush their teeth or use mouthwash for at least 30 minutes prior to their appointment.

Vaccination Side Effects

Common side effects

People very often have tenderness, pain, warmth, redness, itching, swelling or bruising or less commonly have a small lump in their arm where they have been vaccinated.

Other common systemic side effects

Some people can develop these symptoms after vaccination. They usually last for less than a week after you are vaccinated (more commonly 24-48 hours afterwards).

- Fatigue
- Headaches
- Flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills
- Muscle aches
- Joint aches
- Feeling unwell (malaise)
- Feeling sick or nauseated or vomiting

Other less common side effects:

- Abdominal pain
- Decreased appetite
- Feeling dizzy
- Swollen lymph nodes (glands)
- Excessive sweating, itching skin or rash

These symptoms can be reduced by use of paracetamol around the time of immunisation and over the next 24 hours. We would not routinely recommend the use of ibuprofen or other anti-inflammatory medication at this time.

There is some initial evidence from those participants boosted at 28 days, that those participants receiving different vaccines for their prime and boost doses might have some of the listed side-effects more commonly and possibly a bit more severely in the first 24 hours following vaccination. We do not know if this will be the case in participants receiving their boost dose at 84 days.

We would like to try to find out whether there is anything that can be done to reduce these side-effects. To do this, for participants who are due to receive their boost vaccine dose 84 days after their prime vaccine dose, there will be an option to be randomised again either to take paracetamol preventatively for the first 24 hours (with the first dose as soon as is convenient after vaccination), or to take paracetamol only if you feel you need to take it for any symptoms experienced. Dosing should be as indicated in the instructions for this over-the-counter medication and it is important not to exceed the maximum stated dose. We would not supply you with this paracetamol, but would ask you to source it yourself. Taking part in this sub-study is optional, and you do not have to agree.

After immunisation with the BNT162b2 (Pfizer/BioNTech) vaccine, difficulty sleeping has been observed in fewer than 1 in 100 people, and weakness of the muscles on one side of the face has been observed in fewer than 1 in 1000 people.

Serious Reactions

With any vaccination there is a small risk of rare serious adverse events, such as an allergic reaction. These may be related to the immune system or to the nervous system. Severe

allergic reactions to vaccines (anaphylaxis) are rare (approximately 1 per million vaccine doses), but can be fatal. In case of this unlikely event, medication for treating allergic reactions is available and the researchers are appropriately trained in the management of anaphylaxis.

These are new vaccines, and there may be side effects that we are not yet aware of. Following reports of blood clots with lowered platelets after immunisation with the AstraZeneca vaccine a review has been undertaken by the MHRA and the EMA (European Medicines Agency). The reports were into a very rare type of blood clot in the brain, known as cerebral venous sinus thrombosis (CVST), and in some other organs together with low levels of platelets (thrombocytopenia) that might be associated with vaccination with the AstraZeneca vaccine. Up to and including 31 March 2021 there have been 79 UK reports of these blood clots and unfortunately 19 people died. By 31 March 2021 20.2 million doses of the AstraZeneca vaccine had been given in the UK. This means the overall risk of these blood clots is extremely rare, approximately 4 people in a million who receive the vaccine.

The full reports released by MHRA and JCVI can be found at the following links:

https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots

https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement/jcvi-statement-on-use-of-the-astrazeneca-covid-19-vaccine-7-april-2021

Additional side effects to be alert for in the 28 days following vaccination are;

- Sudden severe headache that does not improve with usual pain killers or is getting worse
- An unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- New and unexplained pinprick bruising or bleeding
- Shortness of breath, chest pain, leg swelling or persistent abdominal pain.

Further information about vaccine safety is being actively gathered as the vaccines are being used in the UK and globally. You will be informed of any significant change in the vaccine safety profile.

You will be provided with a 24h trial mobile number. If you experience unexpected events or become in any way concerned you can use this to contact one of the trial doctors at any time. We will ask you to record these symptoms in the e-diary too.

Theoretical risks - Could immunisation make COVID-19 disease worse?

In the past, experimental vaccines were developed by different research groups against the SARS virus, which is in the same family as the COVID-19 virus and also infects the lungs. In some cases, animals that received certain types of experimental SARS vaccines appeared to develop *more severe* lung inflammation when they were later infected with SARS compared

with unvaccinated animals. There has also been one report of this increased disease-associated inflammation being seen in a mouse study for a vaccine against MERS-CoV (another related virus), but this has not been observed in any other reported animal studies, and has not been seen in any of the trials of the vaccines being used in this trial. Importantly, this has not been seen in any of the human studies of these vaccines, which have shown immunisation with the vaccines used in this trial does provide protection against COVID-19 disease.

Will I be protected against COVID-19 from having the vaccines in this trial?

If you participate in this trial you might not receive the same level of protection as that provided by standard vaccinations. The vaccines in this trial have been approved to be protective against COVID-19 when given in the normal way, as a two-dose schedule with the same vaccine. We do not know whether having two different vaccines would give you the same protection against getting COVID-19 as having two doses of the same vaccine, which is why we are doing this trial. We need to know the answer to the question as to whether giving two different vaccines is just as effective as giving two doses of the same one. The answers to this question, which you would be helping us to provide, are really important. There are various reasons why it might not be possible to give two doses of the same vaccine in the future, such as shortage of supply generally or availability at a local level. Participation in the trial will mean that you might receive two doses of the same vaccine or two doses of different vaccines. The results of the trial will allow us to make comparisons between the two possibilities. You will not know whether you have received two vaccines that are the same or different. You should still continue to follow up-to-date national guidelines regarding social distancing and other coronavirus precautions as appropriate.

If you find out that having two different vaccines does not give good immune responses against COVID-19 will you give me another vaccine?

This study is being overseen by a safety monitoring board and a steering committee, who will evaluate part-way through the trial whether there are signs that any of the vaccine combinations are not giving a good enough immune response. If they were to find any sign that any of the different combinations of vaccine were significantly less effective than the standard approach of two doses of the same vaccine you would be informed. We would then take the oversight committee's advice in deciding whether an additional dose of vaccine would be appropriate, and what vaccine this should be, based on all available information at that time.

What if I am eligible for routine immunisation against COVID-19, or become eligible whilst enrolled in the trial?

Participation in this trial means that, unless the trial team specifically advise otherwise, you will not be able to receive any of the approved NHS COVID-19 vaccines in the national programme. It is important to note that participants in this trial will not know which vaccine schedule they have received until after the end of the trial. This procedure is known as

blinding and is a critical part of the trial to avoid bias. For example: If you know which vaccine you have, you might, subconsciously be more or less likely to report certain symptoms. For this purpose, we would not unblind you (tell you which vaccines you received) until the end of the trial, even if you withdrew from the trial, as it would seriously affect our ability to interpret the trial data. We would, however, unblind participants earlier if:

- It became apparent that one schedule was producing an immune response that was thought to be inadequate
- There was an urgent safety need
- Participants were significantly disadvantaged by not being able to know which vaccines they had received in the trial

Of note, the current national guidance for COVID-19 vaccines recommends that individuals who have received two doses of any combination of COVID vaccines do not require any additional doses. This advice may of course change depending on the results of this or other studies.

Therefore, participants becoming eligible for routine immunisation against COVID-19 would not be considered, in itself, a sufficient reason to 'unblind' participants in the trial to check which vaccines they have received.

What are the advantages of taking part?

We anticipate that participating in the trial will mean that you gain some protection against the coronavirus (but cannot guarantee this). It is possible that you could gain this protection sooner than you otherwise would have by waiting for your place in the vaccine roll out. Most importantly, the information gained from the trial will make a valuable contribution to the pandemic response.

What should you do if you believe you may have developed COVID-19 during the trial?

A common and expected side effect of COVID-19 vaccines is fever. If you develop fever in the first 48 hours post-vaccination only, you would not need to self-isolate unless you had other symptoms of COVID-19. If your fever continued (or you had another episode of fever) after 48 hours then you would need to follow the current government advice. We would also ask you to record any fever that you have in your e-diary. If the fever didn't continue, then it is likely that it was a vaccine effect and you can carry on as normal.

Excluding the above, if you develop symptoms that meet the UK government COVID-19 testing criteria, then you must arrange an NHS test as soon as possible, following the normal routes. If this test is positive, you would need to follow government guidance regarding self-isolation as usual. We would also ask you to contact the trial team on com-cov@sgul.ac.uk. If you test positive on an alternative route such as via work or a commercial test then please let the trial team know as well. We may ask you to forward on your test result to us.

If you have a positive test we may invite you for a visit in our clinic which would involve a review by a doctor, a blood test, and a nose and throat swab. This swab would be looking for SARS-CoV-2 but may not be processed immediately – we would not inform you of the result

as it would be a repeat of the positive result you already have. We may have to inform Public Health England of the results of this swab and convey to them details about you including your name as a legal public health requirement. We would also ask you for a nasal fluid sample and optional saliva sample if these are something you have done at other visits.

Please do not attend the clinical trial site until you have been asked by the trial team to do so. Although, in general, you should adhere to government guidance and stay at home when required (for instance during self-isolation or lockdown), attending the trial site for visits during these periods (once asked to do so) is exempt from these rules.

If you are unwell and unable to contact the trial team directly then contact the NHS 111 service or phone 999 if you are severely unwell.

If you are admitted to hospital during the trial then you should inform the medical or nursing staff that you are taking part in this trial. We will provide a contact card for you to give to these staff which will have a link to a website for them to fill in details about your admission. We would also like you to let us know (if you are able) that this has happened.

Do I get access to extra medical treatment from being in the trial?

It is important that you understand that if you do become seriously unwell and need to be admitted to hospital, the standard referral routes within the NHS will be used. Participants will be treated the same way as the general population in this context of the COVID-19 pandemic. We are unable to offer extra medical support outside what is available within the NHS for the general public.

Will I be compensated for taking part in this trial?

Once enrolled you will be compensated for your time, the inconvenience of having blood tests and procedures, and your travel expenses. The total amount compensated will be approximately between **£225-£450** depending on the total number of visits attended. Additional visits will be paid at a rate of £45/visit. Payments will be made following the Day 56 visit, Day 182 visit and Day 364 visit for those having their boost at Day 28. Payments will be made following the Day 112 visit, Day 182 visit and Day 364 visit for those having their boost at Day 84. For those who attend for final screening and vaccination visit (Day 0) but are not eligible to proceed further in the trial, payment will be initiated that day.

Trial reimbursement will be made by bank transfer throughout the trial, so please bring your bank details with you to your screening visit (no cash payments can be made). Should you decide to withdraw from the trial before it is completed, payment will be *pro rata* (you will receive a proportion of the total amount).

What if the area I live in, or where the trial is, goes back into lockdown or high level restrictions?

Travel for visits for trial purposes are exempt from government restriction, as it is considered an essential journey.

What if new information becomes available?

Sometimes during a trial, new information relevant to the trial becomes available. If this happens, we will tell you about it and discuss whether you want to, or should, continue in the trial. If you decide to continue to take part, you may be asked to sign an updated consent form. On receiving new information, we may consider it to be in your best interests to withdraw you from the trial. Your participation in this trial may also be stopped at any time by the trial doctor or the Sponsor for other reasons.

Will I be given proof of immunisation? If "vaccine passports" are introduced will I get one from being in the trial?

At the vaccination visit you will be given a COVID-19 vaccination card which is the same as that used in the national vaccination program. The difference is, unlike in the national program, this card will not give the name and batch number of the vaccine you have received (as this would "unblind" you). Instead, the card will say "COVID-19 vaccine". These cards are not at present considered to be "vaccination passports" - and this is true whether you receive them through the national immunisation programme or through a trial. We are working together with the vaccine task force and NHS digital to ensure that there is a digital record of the COVID vaccines received during the trial, for our participants. Whilst participants remain blinded to which vaccines they have received, we will provide an official letter addressed to "to whom it may concern" stating their involvement in the trial, the premise of the trial and the dates of their vaccines including a statement that they should be considered fully vaccinated in line with the most up to date UK Public Health recommendations.

In order not to disadvantage our participants in a rapidly changing landscape of rules affecting national and international travel as well as event attendance, we will make every effort to liaise with appropriate parties to ensure participants' vaccination status is recorded in the most suitable manner. Should participants still be disadvantaged, then, after further discussion with the Trial Steering Committee, we may unblind all participants to occur not sooner than 28 days after the last trial participant receives their boost dose, if this action will serve to reduce or remove the disadvantage. We will always seek not to disadvantage our participants and will be responsive to any of these kinds of potential changes - taking advice from the trial oversight committees.

Unblinding does not mean that the trial has finished, or that follow up visits have stopped. There are still many very important questions that continued participation in the trial after unblinding can help us answer – most importantly looking at the immune responses to the vaccines received and continued monitoring for safety.

What will happen if I do not want to carry on with the trial?

If, at any time, after enrolment, you change your mind about being involved with this trial you are free to withdraw without giving a reason. If you withdraw we would not usually perform any more research procedures; although occasionally we might need to offer you a follow up visit for safety purposes, for example for blood tests. You would not have to agree to this.

Your decision will not result in any penalty. Unless you state otherwise, any samples taken whilst you have been in the trial will continue to be stored and used for research as detailed above. You are free to request that your samples are destroyed at any time during or after the trial. Your data would be managed as laid out in the section 'What will happen to my data'. If you choose to withdraw from the trial, your standard medical care will not be affected.

What if something goes wrong?

The investigators recognise the important contribution that volunteers make to medical research and make every effort to ensure your safety and well-being. The University of Oxford, as the research Sponsor, has arrangements in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this trial.

In the event of harm being suffered, while the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The trial doctor can advise you of further action and refer you to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment which may be provided if you needed to be admitted to hospital.

Complaints statement

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this trial, you should contact the research investigators who will do their best to address your concerns by sending us an email to com-cov@sgul.ac.uk. Alternatively, you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or the head of CTRG, email ctrg@admin.ox.ac.uk

Would my taking part in this trial be kept confidential?

All information that is collected about you during the course of the research will be coded with a trial number and kept confidential. The information is available to the trial team, authorised collaborators, ethical review committees, St George's University Hospital NHS Foundation Trust, government regulatory agencies and the Sponsor (University of Oxford), who can ask to access the trial data. Responsible independent monitors may be given access to data for monitoring and/or audit of the trial to ensure we are complying with regulations. They are bound by the same confidentiality rules. The electronic diary is sent to you by email to complete online. Your email address will be stored on a secure University of Oxford server, access to the diary system is password controlled and only trial site staff and sponsor IT management can view the email address.

Every effort will be taken to maintain confidentiality. Information about you may be stored electronically on a secure server, and paper notes will be kept in a key-locked filing cabinet or restricted access office at the St George's University Hospital or at the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), University of Oxford. Trial results will be published in a scientific journal but nothing that could identify you will be included in any report or publication. Your de-identified data collected in the trial may also be used in future

research projects that may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide. We would not share anything that could identify you.

If you are not enrolled on the trial, either because you were not eligible after screening or there was not capacity to enrol you, then any data collected will be kept until the end of the trial.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly.

We will be using information from you and your medical records in order to undertake this trial and will use the minimum personally-identifiable information possible. We will keep identifiable information about you such as contact details for 5 years, but with a review of this every 5 years after the trial has finished. This includes a copy of your consent form. The need to store this information for longer will be subject to ongoing review, taking into account the value of retaining this information for participant safety (e.g. to inform participants of unexpected safety signals emerging from post-licensing surveillance), as a resource for the participants (e.g. if they wish to check which vaccines they have received in the study) and any regulatory requirements. De-identified research data will be stored indefinitely. If you have agreed that samples can be retained for future research then your personally identifiable information will be kept with restricted access solely for the purposes of sample management for a minimum of five years after the last sample has been either used or disposed of in order to meet regulatory requirements. Samples will be provided for future research only in a form that does not identify you. We will store research data securely at the University of Oxford indefinitely following removal of identifiable information. If you agree to your details being held to be contacted regarding future research, we will retain a record of this consent until such time as your details are removed from our database but will keep this separate from your research data.

The trial team will use your name and contact details, to contact you about the research trial, and make sure that relevant information about the trial is recorded for your care, in relation to your health during the trial and to oversee the quality of the trial.

At the completion of the trial, unless you consent otherwise (e.g. if you request to be informed of other trials), your personal details will not be used to contact you other than exceptional circumstances concerning your safety. If you consent to take part in another trial carried out by the St George's University Hospital, personal information and medical information including blood test results may be accessed to avoid unnecessary repetition.

Your bank details will be stored for 7 years in line with university financial policy.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those

rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at: https://compliance.web.ox.ac.uk/individual-rights

Note that in order to check that we are conducting the trial to high standards we will be engaging trial monitors, who will have access to your data (including personal identifying information). They will not be retaining data beyond the end of the study. Minimal information about you (not including any identifiable information) may also be shared with third parties such as Public Health England or laboratories undertaking analysis of your blood samples (including, but not limited to, Oxford Immunotec and Nexelis) to help us conduct this research. Retention of data by these third parties will be as per PHE/local policies. Anonymised reports on safety information related to the ChAdOx nCoV-19 (AstraZeneca/Oxford) vaccine will be shared with AstraZeneca.

Some participants will have signed up to NHS Digital's *'Sign up to be contacted for coronavirus vaccine studies'* service. Further information regarding how we will inform NHS Digital of your enrolment in this trial, will be supplied in a Supplementary Privacy Notice for volunteers who are enrolled in the trial.

Involvement of the General Practitioner (GP)/Family doctor (GP)

In order to enrol into this trial, you will be required to sign a form documenting that you consent for us to contact your GP if we need to. This is in case we need to contact your GP to check there are no medical reasons that they are aware of that would make your participation inadvisable. Your GP may be asked to share information about your medical history and give access to any other medical records as required. The researchers will not enrol you in the trial if your GP has relevant concerns about your eligibility or safety.

If you are enrolled in the trial we will write to your GP to let them know this. This will be done regardless of whether we check any medical information with them. It is important to do this so that your medical records are kept up to date.

If you have up to date copies of your medical records or GP summary records please bring these to your screening visit.

What will happen to any samples I give?

If you consent, some of your leftover blood samples can be stored and used for future infectious disease or vaccine-related research in the Oxford BioBank. This is optional; your participation in this trial will not be affected by your decision whether to allow storage and future use of your leftover samples. Upon your request at any time, your remaining blood samples will be destroyed.

Your trial samples will be analysed in the site (hospital) laboratories, Oxford University research laboratories or other specialist laboratories. Other tests to look at the response of your body to the vaccine or to COVID-19 disease will be done with collaborating laboratories in the UK and in other countries, including North America. Any samples or data sent to them

would not include information that identifies you. However, your DNA is unique to you so it can never be completely anonymous.

Will any genetic tests be done?

We would also ask for your permission to store your DNA for research related to infectious diseases and vaccination; you can still take part in the trial if you did not want us to do this.

We are not planning to perform any genetic tests within this trial.

What will happen to the results of the research trial?

The results of this research trial may be presented at scientific meetings or conferences and published in a scientific medical journal. This may not happen until 1 or 2 years after the trial is completed. If you contact the researchers in the future, you can obtain a copy of the results. You will not be identified in any report or publication.

The de-identified data from this trial will be shared with the collaborating partners who are organising and funding this research work. You will not be paid for any part of this. Data from this trial may be used as part of a student post-graduate degree, for example a MD or PhD.

Taking part in future vaccine-related research

With your consent, we would like to keep your contact details after the trial is complete, so we may inform you of opportunities to participate in future vaccine-related research. This is entirely optional and your participation in this trial will not be affected by your decision to allow or not allow storage of your contact details beyond your participation in this trial.

Your details will be stored electronically on a secure server and only authorised individuals at the St George's University Hospital will have access to it. We will not, under any circumstances, share your contact details with any third party institutions without your permission. Being contacted does not oblige you to agree to take part in future research and you can ask us to have your contact details removed from our database at any time.

Who is sponsoring, organising and funding the research? Does the University of Oxford have a financial interest in the results of this trial?

The trial is organised and sponsored by the University of Oxford. The trial is funded through financial support to the University of Oxford from the UK Vaccine Task Force and the National Institute for Health Research (NIHR), which is a UK government funded research agency. Neither your GP nor the researchers are paid for recruiting you into this trial. The ChAdOx1 nCOV-19 vaccine was developed as a partnership between the University of Oxford, who are sponsoring and coordinating this study, and AstraZeneca UK Limited. AstraZeneca holds an exclusive commercial license for this vaccine and has committed to making the vaccine available on a 'not for profit' basis for the duration of the current pandemic. Both parties could potentially profit from this vaccine in the future. AstraZeneca do not have any direct involvement in the conduct of this trial.

Who has reviewed the trial?

This trial has been reviewed by the NHS Research Ethics Service (RES) – South Central – Berkshire and has been given a favourable ethical opinion. The Medicines and Healthcare products Regulatory Agency (MHRA), which regulates the use of all medicines in the UK, has reviewed the trial design and has granted permission to use these unlicensed vaccine schedules in this clinical trial.

Further information and contact details

If you relocate during the course of the trial and would like to continue taking part, it may be possible if there is a trial site nearby that are able to perform the remainder of your trial visits. If this were the case, we may transfer copies of your research notes including consent forms. The responsibility for your continued care in the trial would be transferred to the new trial site.

We hope this information sheet has answered all your questions. If you would like further information about participating in research please visit the following website: http://www.nhs.uk/conditions/Clinical-trials/Pages/Introduction.aspx. For independent advice about participating in this trial you may wish to contact your GP. If you would like to speak to one of our team members to discuss any aspect of this trial or **if you are interested in taking part in the trial, please contact us**:

Vaccine Institute
Room 0.123 Ground floor Jenner Wing
St Georges University of London
Cranmer Terrace
Tooting
London
SW17 0RE
com-cov@sgul.ac.uk

Supplementary Privacy Notice for Enrolled Participants

This privacy notice is for the Comparing COVID-19 Vaccine Schedule Combinations (Com-COV) study participants who have signed up to NHS Digital's *'Sign up to be contacted for coronavirus vaccine studies'* service.

Data Protection

In the course of enrolling in the Comparing COVID-19 Vaccine Schedules (Com-COV) study you have provided information about yourself ('personal data'). We (University of Oxford as Sponsor of the study) are the 'data controller' for this information, which means we decide how to use it and are responsible for looking after it in accordance with the General Data Protection Regulation and associated data protection legislation.

How we use your data

NHS Digital contacted you on behalf of the University of Oxford to invite you to join our Comparing COVID-19 Vaccine Schedule Combinations (Com-COV). This is because you signed up to NHS Digital's '*Sign up to be contacted for coronavirus vaccine studies service*'. You were contacted because you were eligible to take part in our study based on the information you provided to NHS Digital when you signed up to its service (namely your age and geographical location).

You can only be enrolled in one vaccine study at a time. This means we need to let NHS Digital know that you are now enrolled in our study. We will do this so that NHS Digital can update its records and so you are not contacted unnecessarily about any joining any other vaccine studies or inadvertently enrolled in more than one study at a time.

Each site will review which of their participants had signed up to NHS Digital's *Sign up to be contacted for coronavirus vaccine studies'* service. If you had signed up to this service, the site you are enrolled with will share your name with NHS Digital to confirm your enrolment. They will keep a record of having confirmed your enrolment with NHS Digital.

We need to process your data for the above purpose in order to effectively carry out research, which is a task we carry out in the public interest. Data concerning health and ethnicity is special category data, which means that we must meet additional requirements to process it. The additional requirement we meet to process this data is that the processing is necessary for the purpose of research.

We will only use your data for the purposes for which we collected it, unless we reasonably consider that we need to use it for another related reason and that reason is compatible with the original purpose. If we need to use your data for an unrelated purpose, we will seek your consent to use it for that new purpose.

Who has access to your data?

Access to your data will be provided to those who need to view it as part of their work in carrying out the purposes described above.

Where we share your data will with NHS Digital, we will seek to share the minimum amount necessary (please see NHS Digital's privacy notice for how it uses your data).

Retaining your data

Once we have confirmed your enrolment to NHS Digital, we will securely destroy the list of people that NHS Digital contacted about our study on our behalf.

We will retain a record of having confirmed your enrolment with NHS Digital along with other identifiable information about you for 5 years and with a review of this every 5 years after the trial has finished. The need to store this information for longer in relation to licensing of the vaccine will be subject to ongoing review.

Security

Your data will be held securely in accordance with the University's or equivalent St George's University Hospital policies and procedures. Further information is available on the University's Information Security website here.

Where we store and use your data

We store and use your data electronically on a secure server, and paper notes will be kept in a key-locked filing cabinet or restricted access office at the St George's University Hospital or on University premises.

Your rights

Information on your rights in relation to your personal data are explained here.

Contact

If you wish to raise any queries or concerns about our use of your data, please contact us at com-cov@sgul.ac.uk. Alternatively, you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or the head of CTRG, email ctrg@admin.ox.ac.uk