Imperial College London

COVHIC002
COVID-19 HUMAN CHALLENGE STUDY

UNIVERSITY OF OXFORD

COVHIC002 Coronavirus Human Infectious Challenge Study

COVHIC002 is a study to find out the amount of the Delta variant virus that causes COVID-19 infection in young healthy vaccinated adults to understand why some people get "breakthrough" infection and allow future trials of vaccines and treatments.

- We would like to invite you to take part in this research study.
- Before you decide, we would like you to understand why the research is being done and what it would involve for you.
- Please read this Participant Information Sheet carefully. One of our team will then go through this information sheet with you and answer any questions you may have.
- Please watch the video for the study https://www.youtube.com/watch?v=wgt9tdzwEFE
- Please talk to others, including your family, friends and GP about the study if you wish.
- You do not have to take part in this study, and you can change your mind at any time.

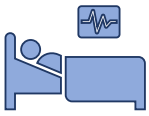
Why are we doing this study?

The SARS-CoV-2 virus is going to be with us for years to come, even with vaccines available. This is partly because many people are getting "breakthrough" infections (i.e. infections that occur in people who have been vaccinated) as new variants appear and immunity wanes. Human challenge studies involve giving volunteers the virus at a specific time (rather than someone catching it naturally). This way we can get very detailed information about the infection and why people respond to infection differently despite identical virus exposure. Some information can only be found in this way and will have important public health benefits. Up to 120 people will enter this study to find out:

- How well the Delta SARS-CoV-2 variant infects previously vaccinated people;
- What levels of immunity mean people are less likely to get infected;
- What happens in "breakthrough" infection with Delta.

This study will pave the way for testing whether vaccines and treatments can make people less infectious to better control the pandemic.

Condition Studied:
COVID-19



Locations:
Oxford

Study Length:
1 Year

Number of Visits:
13-17 Days in Quarantine,
5 Follow Up Visits

Key points you should know before making your choice

- **If you take part in this study, you will be given SARS-CoV-2 virus (the cause of COVID-19 disease) as drops in the nose.**
- **You may develop COVID-19 symptoms, including tiredness, loss of smell and/or taste, cough and fever. These should get better by the time you leave quarantine but some may go on for weeks or more.**
- **If you need for your sense of smell to remain completely normal, you should not enter this study.**
- **There is a very small risk that you could become more seriously unwell if you develop COVID-19, but this is extremely rare in young, vaccinated people. We will go through these risks with you in detail (see Section 3.1).**
- **You will need to stay in an en-suite room in a designated quarantine unit staffed by clinical study staff with no visitors for (on average) 17 days but may be discharged earlier after 13 days if you are not infectious or later if you are still infectious.**
- During quarantine, you will be closely monitored for any symptoms. If these get worse above a certain level, you may be given medicine to treat the infection. If you become unwell with COVID-19 and require more specialist care, you will be transferred to the local NHS hospital.

- If you experience more severe or longer-lasting symptoms, you will be provided with care by medical specialists and can claim on our insurance in case there are any long-term problems.

Follow this link (https://www.hic-vac.org/public-information/human-infection-studies-coronavirus-covid-19) and watch this video (https://youtu.be/FncT4ki-Uww) for further information.

Study Eligibility Criteria

Before reading this Participant Information Sheet further, it may be worth reading the study's key eligibility criteria to assess whether you might be eligible to take part.

Eligibility Criteria:

- ✓ You must be 18-30years old (inclusive) at the time of consent
- ✓ You must be willing and able to commit to the study procedures and visits (which include taking bloods and nose/throat swabs)
- ✓ You must be vaccinated against COVID-19
- ✓ You must be in good health with no clinically significant medical conditions
- ✓ You must have a BMI between 18 and 30 (use the NHS BMI Calculator: https://www.nhs.uk/live-well/healthy-weight/bmi-calculator/)
- ✓ You must have knowledge of your family's significant medical history
- × You must NOT be in close domestic contact (e.g. live with) anyone under 2 years old or anyone who is clinically vulnerable or immunosuppressed.
- × You must NOT have severe allergies or intolerances, for example, to foods or drugs, that cause severe allergic reactions such as anaphylaxis
- × You must NOT be a current smoker (including the use of e-cigarettes)
  - If you are an ex-smoker, you must have quit more than 3 months ago and not smoked more than 5 pack years in your lifetime (use the Smoking Pack Years Calculator: https://www.smokingpackyears.com/)
- × You must NOT currently misuse recreational drugs or have a weekly alcohol consumption of more than 28 units per week (one unit being a half glass of beer, a small glass of wine or a measure of spirits)
- × You must NOT have a significant history of using recreational drugs or excessive amounts of alcohol
- × You must NOT have a history of, or currently active, clinically significant illness. Examples include:
  - Cancer (except basal cell carcinoma)
  - Cardiovascular diseases such as high blood pressure, stroke and heart failure
  - Respiratory diseases such as asthma, COPD and cystic fibrosis
  - Bleeding or clotting disorders
  - Diabetes (Type 1 or 2)
  - Liver or kidney disease
  - Rheumatoid arthritis
  - Epilepsy
  - Any immunodeficiency or autoimmune disease
  - Significant depression or anxiety
- × You must NOT have a family history of a first degree relative aged 50 years or less with sudden cardiac or unexplained death
- × You must NOT have a family history of unexpectedly severe COVID-19 (i.e. requiring hospitalisation) or a family history of clotting disorders
- × You must NOT have a personal or family history of any other severe response to a viral infection

If you are a person of child-bearing potential:

- × You must NOT be currently pregnant
- × You must NOT be planning to get pregnant within 6 months of receiving the study virus
- ✓ You must be willing to use effective contraception, such as the pill, an IUD (the coil), the implant or injection, or you must use condoms, or you must practice abstinence with a heterosexual partner until 6 months after receiving the study virus. This does not apply if yourself or your partner are sterile.
- × You must NOT have been pregnant in the last 6 months
- × You must NOT have been breastfeeding in the last 6 months

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UNIVERSITY OF OXFORD

Study Title:	Development of a SARS-CoV-2 Delta variant human infection challenge model
PIS Version and Date:	Version 3.0 16-MAR-2023
Sponsor:	Imperial College London
Sponsor Reference:	21HH7162
Chief Investigator:	Professor Christopher Chiu Department of Infectious Disease, Imperial College London
Principal Investigator:	Professor Helen McShane Department of Paediatrics, University of Oxford
Study Sites:	Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), Oxford or Oxford Experimental Medicine Clinical Research Facility (EMCRF) (Screening and Follow Up) Oxford EMCRF (Quarantine)

We're providing you with this participant information sheet (PIS) to help you decide whether to join the study or not. It's divided into sections that one of us will go through with you when we meet. Each section begins with a question and a very short summary to start our conversation.

Please read this information carefully so that if you agree to join the study you are fully informed. If there is anything you don't understand, please ask one of the study team.

Before you decide to take part in the study, we will (1) talk you through the key facts from the first page; (2) explain all the details of the study using this PIS to guide us and give you time to discuss your participation with anyone you wish; (3) because there is a lot of information to take in, we will give you a break to think about it and then check your understanding with a quiz; and (4) sign the consent form.

Table of Contents

1. What is the purpose of this study?

The SARS-CoV-2 virus is going to be with us for years to come, even with vaccines available. New variants have appeared, including the Delta variant, that can cause “breakthrough” infection in people despite them having been vaccinated. Human challenge studies involve giving volunteers the virus at a specific time (rather than someone catching it naturally) so we can get very detailed information about the infection. The purpose of the study is to help us better understand how variant viruses cause infection despite previous vaccination so we can develop better ways to tackle new variants and follow up with studies to find better vaccines and treatments in a shorter time that can control further outbreaks.

Up to 120 people will enter this study to find out:

- How much Delta virus is needed to cause infection in vaccinated people
- How long vaccinated people are infectious for after “breakthrough” infection
- What happens in infected people with no symptoms

1.1 What is SARS-CoV-2 and COVID-19?

The SARS-CoV-2 virus is the cause of COVID-19 disease. It has caused a global pandemic and spreads between people either by droplets in the air which have been breathed out by an infected person or through contact with contaminated surfaces. Some people do not experience any symptoms at all but can still transmit the infection, which is why the virus can spread so easily.

The common symptoms of COVID-19 are:

- Fever
- Headache
- Tiredness
- Dry cough
- Loss or change in taste and/or smell
- Sore throat
- Diarrhoea
- Body aches

Some vaccines are now available and many more are still being developed. However, being vaccinated does not reliably prevent people from transmitting the virus. Even with effective vaccines available that prevent severe disease, repeated outbreaks are likely to occur for years to come.

Public health measures such as mask wearing, frequent hand washing, and social distancing have been used to control the spread of SARS-CoV-2 in many countries, but they are not a practical long-term solution. We still urgently need to learn more about how the human body reacts to COVID-19 to develop ways to reduce re-infection and spread of the virus and quickly find out whether newer vaccines and treatments can better stop transmission of the virus.

1.2 What is the SARS-CoV-2 (COVID-19) Human Challenge Study?

The purpose of this study is to better understand how variants (the Delta variant in this case) cause infection in previously vaccinated people and follow up with studies to find vaccines and treatments that better block these “breakthrough” infections.

In this study, volunteers will be infected with SARS-CoV-2 (the “study virus”). This study will recruit up to 120 healthy, fully vaccinated volunteers aged 18 to 30. The participants will be given the Delta variant of the SARS-CoV-2 virus by drops in the nose.

If you take part, you will be **deliberately given SARS-CoV-2 and may develop COVID-19.** Living in the UK, you already face a risk of being exposed and infected naturally, although this will be with a different variant to the ones in this study. During this study, you will definitely be exposed to the Delta strain and may develop infection.

The information obtained from this study will allow us to:

- ✓ Define under what conditions the Delta variant can cause “breakthrough” infection
- ✓ Clearly show when vaccinated people become infectious and when they stop being infectious
- ✓ Start studies that will test new (and hopefully better) vaccines
- ✓ Start studies to test whether treatments work to reduce the amount of virus
- ✓ Better understand what happens in the body during COVID-19 in vaccinated people and why that differs between individuals

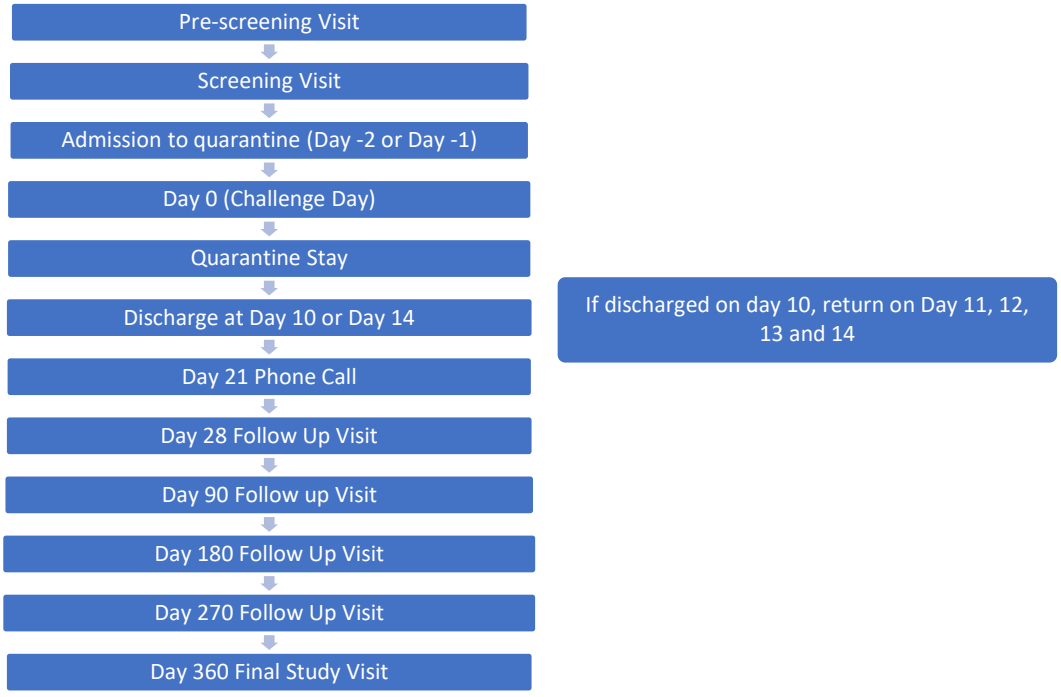
The main part of the study will take place in the quarantine unit at the Oxford EMCRF, where you will be staying in isolation in your own en-suite room. You will need to check into the quarantine unit 2 days before you are given the virus (known as Day -2). You will be deliberately infected with COVID-19 on Day 0.
If you remain uninfected, you can leave the quarantine unit ten days later (Day 10), but will be required to attend the Oxford EMCRF on Day 11, Day 12, Day 13 and Day 14. If it is difficult for you to attend these visits from home you may be able to stay in the quarantine unit until Day 14 if agreed in advance with the study team but you would need to stay in your room.
If you become infected, you will be required to stay in the quarantine unit until at least Day 14. You can be released from quarantine on Day 14 if you meet the discharge criteria (which make sure you are not infectious to others). If there are signs you may still be infectious, you will need to remain in the quarantine unit for a few extra days until you meet the discharge criteria, to limit the risk of the virus spreading.

<u>If you participate in the COVID-19 study:</u>

- **If you take part in this study, you will be given SARS-CoV-2 virus (the cause of COVID-19 disease) as drops in the nose.**
- **You may develop COVID-19 symptoms, including tiredness, loss of smell and/or taste, cough and fever. Mostly these will get better by the point you go home from quarantine, but may last for several weeks or more.**
- **There is a very small risk of becoming more unwell if you develop COVID-19 illness, but this is extremely rare in young people (please see Section 3.1 for details).**

- You may be asked to self-isolate prior to admission to the Oxford EMCRF
- You will be admitted to the quarantine unit 2 days prior to you being given the virus.
- After being given the virus, you will need to stay quarantined on your own in a single en-suite room for 10-14 days. If you are still contagious (you could infect someone else), you may have to stay longer, usually a few more days at most.
- You will not be able to have visitors. The only in-person contact will be with the research team. You can bring in personal devices such as phones, laptops and tablets to watch films, study work etc and to call friends and family.
- If you take part, you will consent to have study assessments and procedures at each visit and every day during the quarantine, including giving blood samples and swab samples from your nose. Some of these will be done multiple times each day (see Appendix 1)
- If you withdraw your consent and decide to "leave the study", you will be very strongly encouraged to remain in the Quarantine unit until you are no longer contagious and will need to remain in self-isolation according to government guidelines at the time.
- After you are discharged from the quarantine unit, we will check on your health with at least 5 follow up visits over about 1 year from being infected. These will take place at the CCVTM or at the Oxford EMCRF.
- You will be given an emergency telephone number and other contact details for the study team in case you have any questions or concerns at any time.

Overview of the study visits



1.3 Why is the COVID-19 Human Challenge model so important?

The SARS-CoV-2 virus is going to be with us and causing disease for years to come, even with vaccines that are currently available. There are many aspects of COVID-19 infection that scientists still don't understand. Human challenge studies involve giving a defined amount of the virus to individuals at a specific time (rather than people catching it naturally) which means we can get very detailed information about the infection. Some information about viruses can only be found in this way. We believe that the knowledge obtained by studying infection of vaccinated volunteers will have important public health benefits and play a major role in the ongoing management of the pandemic as it moves into a new stage:

1. **Despite vaccination, some people still catch the virus and get sick while others do not.** Human challenge is the only way to clearly show what factors differ between individuals as participants are all given the same virus in the same way. Any differences between those who do and do not get infected must then be due to factors within them and not the virus or environment. Important findings from this study will include what level of different types of immunity protects people from re-infection. This may help us find new ways of protecting people and to predict how good new vaccines are.

2. **Quicker testing of new vaccines and antiviral treatments that can block transmission is still urgently required.** One of the key questions we still have is how to make vaccines that prevent people carrying and spreading the virus (which current vaccines are not good at) as well as stopping people from getting ill. This study will establish the best way to run future studies that more quickly find out whether new vaccines or treatments can reduce infectious virus coming out of the nose so doctors can focus on the vaccines most likely to block spread of the virus to others.

3. **Understanding how immunity following vaccination affects risk of infection and infectiousness will allow better vaccines and treatments to be made.** Human challenge studies allow us to accurately measure how long people are infectious, from first being exposed to the virus to when the virus is no longer detectable. People can be infectious before they start to feel unwell (have symptoms) and this is a critical period that affects whether people will become sick. Human challenge studies are the only way to accurately know when infectiousness starts as we know exactly when the person gets the virus and what happens before they have symptoms.

4. **Vaccination increases the proportion of people who get no symptoms (asymptomatic) from a coronavirus infection but how this happens is not well understood.** This might be something to aim for with better vaccines or medicines as it is better than getting sick with COVID-19, but these people are still major spreaders of the infection because they don't know they are infected. Human challenge is the only way to find out what is special about these asymptomatic people since normally they would never even know they had the infection.

2. Why have I been given this participant information sheet?

We are inviting you to take part in this study because you have expressed an interest in the study and meet some of the initial criteria. Before participating in this study, we need to make sure that you fully understand and agree to what is going to happen and that you are healthy and unlikely to get severely ill from the virus.

Please make sure you read and understand this participant information sheet before you make the decision to take part. If you have any questions or concerns, please ask a member of the study staff and, if you want to, discuss any of this information with your family, friends, and your General Practitioner (GP) before you decide to take part.

For this study, we aim to recruit up to 120 volunteers who are healthy, aged between 18 – 30 years and who are fully vaccinated against COVID-19.

Please initial this box to confirm you have read and understood **Section 1 and 2**	

3. What are the risks of taking part?

3.1 What are the risks from the study virus?

The SARS-CoV-2 virus is still causing a world-wide pandemic of respiratory disease that ranges from no symptoms or mild illness to severe respiratory disease that may also affect other parts of the body. Around a third of unvaccinated people infected with COVID-19 experience no symptoms at all.

Without vaccination, most severe cases of COVID-19 disease are in the elderly (over 65 years of age) and those with pre-existing medical conditions (such as diabetes). Having had a full course of COVID-19 vaccine is highly effective (>90-95%) at preventing severe COVID-19 disease even with variant strains.

While it is not possible to predict completely accurately the risks to you from participating in this study, we now know a lot about the disease since the virus emerged in late 2019. In addition, a SARS-CoV-2 human challenge study was carried out in 2021 so we have a guide for what to expect.

The type of virus you will be given in this study will be a variant of the COVID-19 virus (the Delta variant) which came to the UK in around March/April 2021. COVID-19 vaccines that have been given in the UK are highly effective at preventing severe disease from the Delta variant.

The delta virus that will be used in the challenge study was originally obtained by swabbing a healthy person in the UK with mild COVID-19. From this sample, the virus was grown in ultra-clean conditions in a lab and tested in the same way as licensed medicines and vaccines to create a larger batch that is free from other infectious organisms or contaminants. This is done in a specialist unit that is certified and follows UK regulations. In the earlier human challenge study, 36 volunteers who had neither been vaccinated nor known to have had previous infection were given the original “Wuhan-like” COVID-19 virus produced in an identical way at the same specialist unit. This study will be the first time that the Delta variant virus is used in a challenge study.

In the first challenge study with the “Wuhan-like” virus, all infections were mild, with most infected participants developing symptoms that peaked after about a week and then got completely better. Nobody required treatment for more severe symptoms with most participants back to normal by the time they were sent home and 2 out of 18 infected volunteers having no symptoms at all. Reduction in sense of smell and/or taste were common but in most affected participants this was back to normal within a month. One person still had some reduction in their sense of smell 9 months after they were infected, but this steadily improved throughout that period and had resolved by the end of the study. Vaccination is known to reduce the likelihood and severity of symptoms, with “long COVID” symptoms halved in some studies, so these symptoms are likely to be less in this study as all participants will have been vaccinated. In addition, during that study, participants were asked to carry out several reaction time, reasoning and memory tests every day. These showed small differences in a minority of the test scores between infected and uninfected groups, with lower scores on average mainly in the Object Memory tests after infection. None of the participants described symptoms related to these changes, with these differences fluctuating towards the end of the quarantine and afterwards. What these differences mean is currently unclear as these research tools have not been fully tested in the context of infection. Much bigger studies will need to be done to see if differences of this type and size have any impact on health. Changes like this have also been seen after common colds as well as COVID-19 in the community earlier during the pandemic. These studies generally suggest that test scores normalise with time. Such differences are much less in preliminary data from those with Delta infection in the community, so may be less likely to be seen in this study.

3.1.1 What symptoms are there likely to be related to infection?

If you do get symptoms, you are most likely to experience one or more of the following during the study:

- You may have flu-like symptoms including:
  - Stuffy nose
  - Sneezing
  - Sore throat
  - Runny nose
  - Headache
  - Tiredness
  - Muscle/joint aches
  - Cough
  - Fever
  - Change in sense of smell/taste

Reduced sense of smell (anosmia) is a common symptom of COVID-19. Most people who experience a loss or change in their smell from COVID-19 recover quite quickly, but some people can experience this reduction in or altered sense of smell for longer periods of time (months). However, earlier in the pandemic it was been shown that 96% of people with COVID-related smell problems have normal sense of smell by 12 months. Since then, vaccinated people have been seen to be substantially less likely to suffer changes in their sense of smell following infection. However, if you were to experience prolonged loss of or altered sense of smell from being given the study virus, the study team will ensure you get the necessary care and treatments and can refer you to a specialist. If you need your sense of smell to remain completely unaffected, such as for work, then we will ask you not to take part in this study.

3.1.2 What is the risk of "long COVID"?

In most cases, symptoms in younger adults get better within 3 weeks. However, some people have longer-term symptoms that can last for months. This is sometimes called "long COVID". Those who are older, female, in poor general health and had a larger number of symptoms at the time of their infection appear to be at higher risk of long COVID. The risk of long COVID is very much reduced in vaccinated people. The most common long-lasting symptoms are:

- Tiredness
- Breathlessness
- Palpitations (racing heart)
- Chest pains
- Joint or muscle pain
- Not being able to think straight or focus ("brain fog")
- Loss or change in smell/taste.

In most cases, these changes go away after a few months, but it is still not completely clear exactly how long these symptoms can last for and how many people they might affect.

As a healthy adult aged 18-30 who has been vaccinated, your risk of long COVID is low: around 1-2.5% (1 to 2.5 people in 100) aged 18-30 in the UK still reported symptoms (most commonly tiredness, weakness, difficulty concentrating and loss of smell) more than 12 weeks after their infection. These symptoms were often mild, with only 0.5-0.6% (around 1 to 1.5 people in 200) reporting that the symptoms interfered with their daily activities. Some of these people will have been infected before they got vaccinated, and some will have pre-existing medical conditions, so the risk for a screened volunteer is expected to be lower.

People who have been vaccinated against COVID-19 are relatively protected against developing long COVID. Studies have estimated that the risk of long COVID in younger people who are vaccinated was reduced by around 20-50%.

After the earlier SARS-CoV-2 human challenge study the only longer-lasting symptom was reduced sense of smell. We will monitor your sense of smell and any symptoms of long COVID during the follow-up visits. If you have drawn out symptoms, we will refer to you specialists and give you the best possible treatment.

It is also important to note that long-lasting symptoms aren't unique to COVID-19 and can occur after other viral illnesses.

3.1.3 What is the risk of severe disease?

In young adults, severe disease due to COVID-19 is very uncommon even without vaccination and reduced by up to 95% following a full vaccine course. Based on estimates of risk from the general public aged 18-30 before vaccines were available and 95% reduction in risk by vaccination:

If you pictured the number of affected people in Wembley Stadium (which holds 90,000 people), this would equate to:

- **Risk of death** following infection: between 0 and 1 person in a full stadium
- **Risk of ICU admission** following infection: between 0 and 2 people in a full stadium
- **Risk of hospitalisation** following infection: between 3 and 18 people in a full stadium

The risks will be even lower for volunteers taking part in this study not only because all volunteers will be fully vaccinated against COVID-19 but also as the health screening will ensure people with underlying health conditions (who are at higher risk of becoming severely unwell) do not take part.

We do not expect you to become very unwell with COVID-19 but we will be monitoring you closely during the quarantine period. If you start to become unwell or your tests show that you might be becoming more severely ill, we will assess you, give you immediate treatment (see Section 3.2) and may decide to move you from the Quarantine Unit into a clinical ward within the Oxford EMCRF. You would be given the most appropriate treatment according to your specific medical needs. These might include extra oxygen, steroids (that reduce inflammation in the lung) and antiviral medicines. If you need more intensive care, such as help with your breathing, this will be provided to you in the main hospital.

More serious risks from COVID-19 infection are listed below. These occur in less than 1 in 10 people who are infected and mostly in older people, but are extremely rare in vaccinated young adults.

- You may develop shortness of breath and the oxygen levels in your body may drop.
- You may develop pneumonia (lung infection). You may then need to receive extra oxygen by mask or by placing small tubes near your nose.
- You may struggle to breathe on your own. In this case, you may be given help with your breathing using a ventilator (a mechanical breathing machine). About one-half of patients who reach this state of severity will die but this is very rare in young healthy adults.
- Although the risk is small, you could develop low blood pressure or shock. If this happens you will be given medication and other support to maintain your blood pressure. Treatments for shock in COVID-19 are not always successful, and death is in such circumstances regrettably common.
- You may develop blood clots. These could cause swelling in your legs, or they could (rarely) lead to a stroke. A stroke is when a blood vessel that brings oxygen and nutrients to your brain becomes blocked by a clot, or the blood vessel ruptures. A stroke may be minor, or it may be more serious, leading to paralysis of one side of your body, inability to speak, or other serious nervous system problems. These outcomes from a stroke could be long lasting or even permanent. If you have a stroke, you could be permanently disabled or you could never recover your full strength, or, in a few instances, you may die.
- In rare circumstances there may be kidney damage. Normally this gets better but permanent kidney failure may require use of an artificial kidney system (dialysis) or may require that you receive a kidney transplant.
- You could develop liver disease (your liver will not work as well). Normally this gets better but it could be permanent. Severe liver disease can be fatal or require a liver transplant.

- You may develop a newly described complication in which the body's immune system turns against your body's tissues (called paediatric inflammatory multisystem syndrome or PIMS-TS), damaging blood vessels, the skin, and other organs. However, this syndrome is seen almost exclusively in children and teenagers.

3.1.4 What are the risks of transmitting the virus to other people?

The SARS-CoV-2 virus is very contagious. However, after you have been given the virus, you may remain uninfected and be informed that you can leave the quarantine unit at Day 10. If that is the case, you will be advised to just follow the current government guidance on infection prevention and control measures such as mask-wearing and handwashing after you leave the quarantine unit.

If you become infected during quarantine, you will need to remain for at least 14 days post challenge to prevent spreading COVID-19 to the community. **In case you wish to withdraw your consent and "leave the study", we will talk to you again in detail about the importance of remaining in the quarantine unit until you are no longer contagious. This is for both your safety and that of others.**

You will be tested for the COVID-19 virus in your nose and throat every day while in the quarantine unit. Regardless of whether you become infected or remain uninfected, you must remain in your room, and you are not allowed to have visitors. Friends and relatives may leave things for you at the quarantine unit but are not allowed to enter. You are not allowed to send materials out, such as mail or packages, while you are in the quarantine unit as these may have virus on them.

Remaining in the quarantine unit will also allow close monitoring by the study team. If you must leave the quarantine unit before you have been discharged, you will be strongly advised self-isolate at home until you are no longer infectious. If you return home and there are other people in your household, they will also be advised to self-isolate to limit any possible spread of the infection. The study team will inform you of any relevant government guidelines or policies on self-isolation and infection control before you leave.

3.1.5 What are the potential harms to an unborn child?

We do not know how COVID-19 affects an unborn baby, so you cannot be in the study if you are pregnant. If you are likely to become pregnant during the study (including the follow-up period after quarantine), you should not take part.

You must notify the study doctor if you or your partner become(s) pregnant during the study. If you do become pregnant, your study participation will be stopped, your pregnancy will be monitored, and we will follow up on your health to ensure there are no long-term complications.

If you are female:
You must not donate eggs within 6 months of being given the study virus,
You must agree to use an effective method of contraception from 2 weeks before to 6 months after viral challenge.
Acceptable methods of contraception include:

- the coil
- female sterilisation
- oral, injected or implanted hormonal methods of contraception
- barrier methods such as condoms
- true abstinence from heterosexual sex
- Female participants with a vasectomised male partner, where the vasectomised male is her sole partner.

If you are male:
You must not donate sperm within 6 months of being given the study virus.
You must agree to use an effective method of contraception from the date of viral challenge to 6 months after viral challenge including:

- barrier methods such as condoms
- true abstinence from heterosexual sex

The study doctor will discuss the birth control methods allowed during the study and for the period of time they will be needed after viral challenge. Please share this information with your partner and talk to your GP or the study staff to decide the best method of birth control.

3.2 What are the risks from "rescue" treatment?

To help prevent volunteers going on to suffer severe disease, an antiviral treatment may be offered to you if you develop symptoms or other features (such as a severe persistent cough or high fever for a long time) above a certain level and if the study team believe this would benefit you.

Potential treatments include:

1. **Paxlovid (PF-07321332/ritonavir):**
   - Is an antiviral drug (a drug that stops the SARS-CoV-2 virus from multiplying) developed by Pfizer.
   - It has been given conditional approval by the MHRA in the UK for treating COVID-19 patients who are at risk of progression to more severe illness.
   - We have secured a stock of Paxlovid for use in this study should it be required. This would be the treatment you would most likely receive, and it is the preferred treatment to be used.
   - It has not been used to treat young healthy people in the early stages of infection, so we cannot be sure how useful it is in this situation. However, there are grounds to think it might work. It has been shown to be safe and cause few side effects in adults. In people at high risk of severe COVID-19, it has been shown to reduce hospitalisation and severe disease if given earlier.
   - Is taken as an oral tablet.
   - Common side effects (up to 1 in 10 people):
     - Diarrhoea
     - Vomiting
     - Altered sense of taste

You can find the patient information leaflet for Paxlovid here:
https://www.medicines.org.uk/emc/product/13145/pil

Paxlovid can reduce the efficacy of some combined oral contraceptive pills, therefore all women using the combined oral contraception pill will also need to use a barrier method of contraception during treatment and for 30 days after stopping Paxlovid. The study doctor will discuss all of this with you in detail should it apply to you.

2. **Lagevrio (Molnupiravir):**
   - Is an antiviral drug developed by Merck. It has been given conditional approval by the MHRA in the UK.
   - Is taken as an oral tablet.
   - Common side effects (up to 1 in 10 people):
     - Diarrhoea
     - Nausea
     - Feeling dizzy
     - Headache

You can find the patient information leaflet for Molnupiravir here:

https://www.medicines.org.uk/emc/product/13044/pil

3. **Veklury (Remdesivir):**
   - Is an antiviral drug developed by Gilead Sciences. It has been given conditional approval by the MHRA in the UK.
   - Common side effects (up to 1 in 10 people):
     - Nausea
     - Headache
     - Rash
     - Side effects associated with the infusion site such as brief pain, bleeding, bruising of the skin, soreness, swelling and possible infection at the infusion site.

You can find the patient information leaflet for Remdesivir here:
https://www.medicines.org.uk/emc/product/11597/pil

It is unlikely that we will use molnupiravir or remdesivir during the study. If you were to receive these drugs, the study doctor would provide you with further information at the time.

2.2.1 Allergic Reactions

Allergic reactions to the intervention treatments could happen. You will be monitored by medical professionals at the time that you are given the drug to watch for any allergic reaction. Serious allergic reactions that can be life-threatening may occur but are rare.

Some signs of allergic reaction include:

- rash
- difficulty breathing
- sudden change in blood pressure
- swelling around the mouth, throat, or eyes
- fast pulse
- sweating

Treatment for severe allergic reactions will be immediately available whenever intervention treatment is being administered.

3.3 What are the risks from ionising radiation?

If you take part in this study, you will have a chest X-ray at the screening visit. This is not a procedure you would otherwise have and therefore exposes you to ionising radiation. This procedure uses ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. Taking part in this study will add only a very small chance of this happening to you. The chest X-ray will be reported by an NHS Consultant Radiologist and any abnormal findings will be appropriately followed up, with referral to specialists where required.

The study doctor will be able to provide you with further information about the risks associated with these radiological assessments.

3.4 Are there any other risks of being in the study?

- You may become **anxious, lonely or depressed** by being confined to the Quarantine Unit for many days without being able to see family or friends. The study team will try to provide comfort if this is the case, and you will be able to make phone and video calls with your friends and family.
- Your personal **private space will be limited**, and you will be visited frequently by study staff to check on you.
- Some of the tests or procedures in the study may be **stressful or make you worried** about how others might see you, such as concern about being tested for HIV.
- We will tell you as soon as possible if we become aware of **new information** that could change your mind about taking part in the study.

- If you have any **insurance policies**, you should check whether taking part in this research study affects them.
- If you receive **state benefits** you should check if the compensation received from taking part in this study affects any state benefit payments to which you are entitled.
- You should carefully consider the risks involved in taking part in clinical research in the context of your career choices, as **long-lasting symptoms may affect your work**. If you do experience symptoms that impact your work, compensation arrangements are detailed in Section 7.2.
- Drawing blood may cause slight pain and occasionally bruising at the site where the needle enters. Rarely, people feel light-headed or even faint.
- Nose and/or throat swabs are not painful but can be uncomfortable. Swabbing the back of the throat can cause individuals to cough or gag. The deep nasal swab (and nasosorption tests) can make your eyes water or rarely cause nose bleeding.

Please initial this box to confirm you have read and understood **Section 3**	

4. Do I have to take part?

No, taking part in research is entirely voluntary. It is up to you to decide whether or not to take part.

If you are not eligible to take part, you will be contacted by post, email or phone, thanking you for your time and explaining that you were not eligible.

If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. You will be paid for the time you have spent in the study (see Section 5.5).

4.1 What should I do if I want to take part?

If you have not done so already, you will need to register your interest in taking part in the study with the study team by visiting the https://trials.ovg.ox.ac.uk/trials/covhic002 to complete an online pre-screening questionnaire and submitting your details if you are eligible, or by contacting the study team directly at covid19-challenge@paediatrics.ox.ac.uk . The study team will then contact you to discuss the study in detail and answer any questions you may have about the study and ask you some further questions relating to your eligibility for the study. Following this discussion with the study team, you may then be invited for a pre-screening visit (see Section 5.1.1).

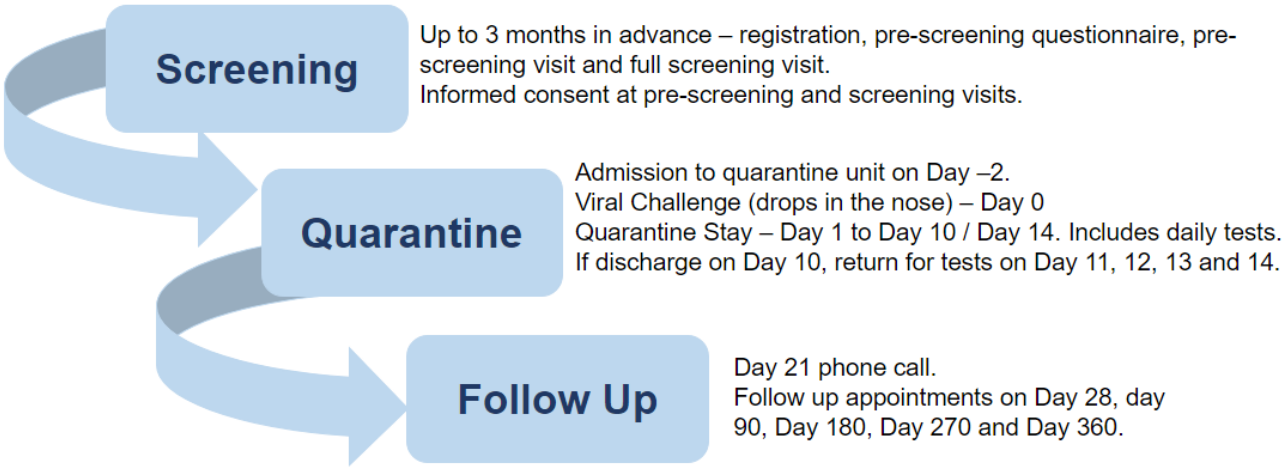
Please initial this box to confirm you have read and understood **Section 4**	

5. What does the study involve?

The study will aim to recruit up to 120 volunteers. Each person will be given a small amount of virus by drops in the nose. Some participants will remain uninfected after being given the virus, while other participants become infected. The study follow up will continue for 1 year.

5.1 Study Design

There are 3 main stages of this study.



5.1.1 Pre-Screening

Once you have registered your interest in taking part with the study team, either by completing the online pre-screening questionnaire, or by contacting the study team directly, your details will be added to a database along with your health information. The study team will then contact you by phone to ask further questions pertaining to the full study inclusion/exclusion criteria. If inclusion/exclusion criteria are provisionally met based on answers to these questions, they will then invite you for a pre-screening visit and send a confirmation email with the visit details.

Pre-Screening visits will be conducted at the CCVTM/ Oxford EMCRF. The study team will discuss the pre-screening process with you and answer any questions you may have. If all your questions have been answered and you would like to go ahead with the pre-screening visit, the study doctor or nurse will ask you to read, sign and date the pre-screening consent form. They will then also sign this consent form and provide you with a copy.

Following informed consent, the following assessments will take place at the pre-screening visit:

- Confirmation of your name, age, gender, and contact details
- Blood sampling for Anti-S and Anti-N serology (SARS-CoV-2 antibodies)
- Check your COVID-19 vaccination record and ask about your COVID-19 infection history
- *Optional: Dried blood spot capillary sample by finger prick (SARS-CoV-2 antibodies).*

See Table 1 for further information on the tests and procedures that are done at this visit.

Once the results of the antibody tests have come back, if you are still eligible to take part, you will then be invited for a full screening visit. If you are not eligible the study team will contact you

by phone, email or letter to explain the outcome of the antibody test results and thank you for your interest in taking part in the study.

You will not be paid for attending this initial pre-screening visit.

5.1.2 Screening

Screening visits will be conducted at the CCVTM/ Oxford EMCRF. These visits can happen up to 90 days in advance of admission to the quarantine unit for viral challenge. First, the study team will discuss the full screening visit process and the main study with you and answer any questions you may have. If all your questions have been answered and you would like to go ahead, the study doctor or nurse will ask you to read, sign and date the relevant consent form. They will then also sign this consent form and provide you with a copy.

Following informed consent, the following assessments will be completed at screening:

- Full medical and medication history including questions about past and present health including clinically significant family history
- Questions about current weekly alcohol and/or smoking consumption and use of any recreational drugs
- Check of any current or previous participation in clinical trials via The Over-Volunteering Prevention System (TOPS).
- Examination for signs of illness or disease (a physical examination).
- Height and weight measurements to calculate BMI
- Pulse rate, blood pressure, temperature and breathing rate checked (Vital Signs).
- Electrocardiogram (ECG)
- Urine samples to test for:
    - Evidence of infection or kidney/urinary tract conditions
    - Pregnancy (for women of childbearing potential)
    - Drugs of abuse & nicotine
- Blood samples obtained for:
    - Safety blood tests, including full blood count, renal and liver function tests.
    - Hepatitis B and C and/or HIV (the virus that causes AIDS)
    - Human leukocyte antigen (HLA) typing (if you consent to genetic analysis)
- Lung function test (spirometry)
- Nose and throat samples
- Chest X-Ray
- Quality of life questionnaires including the GAD-7 Anxiety Test questionnaire and PHQ-9 Depression Test questionnaire.

See Table 1 for further information on the tests and procedures that are done at this visit.

You will be asked to bring proof of your National Insurance Number and ID with you to this visit. If you do not have a National Insurance Number, you will need to bring your passport. This is so we can check and register you on The Over-Volunteering Prevention System (TOPS).

We will also need to review your medical history records. Sometimes, the study doctor or nurse can review a summary care record for you on the hospital's electronic patient records system (called Cerner). The study team will not look at this until you have signed the informed consent form and discussed any relevant history with the study doctor first.

The study doctor can then review this record with you during the visit and discuss any other relevant medical history.

If we cannot find your medical records on this system then the study team will send a letter and enclose your consent form to your GP practice so they can send us a summary.

After the screening visit, we will also contact your GP to request your medical history to verify the medical history you provide at the screening visit. Once all the test results and the GP summary has come back, the study team will review everything to determine if you are eligible to take part in the study. After deciding to take part in this initial screening, you can still change your mind at any time and withdraw from further assessments and study participation.

If, based on the screening results, you are eligible for the study, you will be invited to take part and a date will be arranged with you to be admitted to the quarantine unit at the Oxford EMCRF. If you are not eligible, because the test results have identified something that makes you ineligible for the study, the study team will discuss this with you. If any abnormal results are found and deemed clinically significant, we will ask for your permission to inform your GP so they can arrange to follow up with you. Future mortgages, travel insurance, private healthcare or life insurance may be affected if a previously unrecognised problem is found during screening.

You will be paid £70 for your time for attending a screening visit.

For the majority of participants, the pre-screening and screening visits will be conducted separately so that the results of the antibody tests from pre-screening can be confirmed prior to you attending a screening visit. There may be some instances, depending on the quarantine cohort you will be joining, that these visits could be combined. The study team will inform you of this when booking you in. You will still only be paid £70 for your time for attending a combined pre-screening and screening visit. You will not be able to choose if your pre-screening and screening visits can be combined.

5.1.3 Pre-Admission to Quarantine Unit

If you are proceeding to take part in the study, a date will be arranged with you to be admitted to the quarantine unit at the Oxford EMCRF days prior (known as Day -2) to you being given the study virus (Day 0). Depending on current guidelines at the Oxford EMCRF, at the time of your admission to the quarantine unit, you may be asked to self-isolate (stay at home) prior to admission. You will be informed by the study team whether this is a requirement before your stay.

Similarly, dependent on the current guidelines at Oxford EMCRF, you may also be required to take a COVID-19 PCR or Lateral Flow Test prior to your admission to the quarantine unit. The study team will assist you in arranging this. If your test result comes back positive, you will no longer be able to participate in the study. If the result comes back negative, your admission date will be confirmed with you.

5.1.4 Quarantine and Challenge Phase

When you arrive at the quarantine unit, a study team member will check you into the room that will be yours for the duration of the stay and check you are happy with the upcoming quarantine and schedule. We will review your eligibility to take part once more. It is possible that the results from the earlier screening visit will require extra tests or some assessments to be repeated to confirm if you can take part. From admission on Day -2 until you are discharged, you will be fully isolated and not able to leave this room. The only face-to-face contact will be with the study team.

The study team will provide you with a schedule, so you know what tests/procedures will be carried out each day. This will help you organise your daily routines during the quarantine period.

Photos of a room with en-suite bathroom at the Oxford EMCRF quarantine unit.

When you arrive at the quarantine unit, we will perform some checks to confirm that you are still healthy, free of any active infection and suitable for the study. These tests will include ECG, mouth and nose swabs (to look for evidence of different types of viral illness including COVID-19 infection and additionally for research purposes), blood tests, vital signs (including weight, pulse, blood pressure, breathing rate, oxygen level measurements and temperature), physical examination and urine tests (including urine screening for drug misuse and nicotine use). Women of child-bearing potential will have a blood test to check for evidence of pregnancy. Mental health assessment questionnaires may be performed at the study team's discretion to assess your well-being.
If there are no abnormalities in these tests and you remain well in the first 2 days in the quarantine unit, we will proceed with the challenge (deliberate infection with SARS CoV-2 virus). If we identify any abnormalities, we may cancel or postpone your quarantine stay. Additional baseline research procedures will be carried out on Day-1 including smell testing, cognitive assessments and mask wearing samples.

Two days after you check into the quarantine unit, the study team will give you the study virus, this will be known as "Day 0". Using a pipette, they will drop small amounts of liquid containing the study virus into each of your nostrils whilst you are lying on your back. After receiving the nose drops, we will keep a close eye on you to check that you do not feel unwell or have any side effects. Once you have received the virus, you will be treated as if you are contagious and study staff will be required to wear full PPE when in your room. The study team will monitor whether you become infected or remain uninfected but may not share this information with you until near the end of the quarantine.

In the first SARS-CoV-2 challenge study, on average, the virus took less than 2 days to start showing up in the nose.

In the quarantine unit, staff will wear protective clothing to prevent the spread of infection. We will also ask you to wear a mask when staff members are in the room to reduce risk of spreading the virus.

We expect that most participants who become infected will develop either no symptoms or only mild symptoms. It is possible to be infected but feel completely well. There is also a small possibility of becoming more unwell, although we think this is unlikely. If you become more unwell, you could be given an antiviral treatment that has been shown to be effective at improving symptoms of COVID-19, if a doctor feels it is necessary (see Section 3.2). The study doctor will discuss with you any treatment that may be used and what it is for before you receive it.

If you become infected, you may "shed" virus from your nose or mouth for 10 days or more through breathing, talking, shouting, and singing, even if you have no symptoms. For this reason, you will need to stay in your allocated room for a minimum 14 days after being given the virus. You may be asked to stay longer if you are still contagious, or the study doctor thinks it is necessary. Some people with COVID-19 can remain PCR positive with a low amount of virus for a longer time but are not contagious. If you remain PCR positive at discharge, you will be provided with a PCR swab kit to take home and asked to perform a PCR swab on Day 21 and use a pre-paid envelope to post it back to the study team. If this is still positive, we will also perform a PCR swab at the Day 28 visit and provide you with further PCR swabs to take home and perform weekly, until you have a negative test. If any of the PCR tests suggest you have more virus than expected, you will be asked to take a lateral flow test to see if you have a current COVID-19 infection. You will not be required to isolate unless the lateral flow test is positive.

If you remain uninfected after being given the study virus, you may be discharged from the quarantine unit on Day 10. You will need to attend the Oxford EMCRF for samples and assessments still on Day 11, Day 12, Day 13 and Day 14. You may be able to stay in the quarantine unit until Day 14, for instance, if attending the Oxford EMCRF for 4 consecutive days is logistically difficult for you. However, this is at the discretion of the study team and will need to be agreed to prior to your admission. If you do stay, you will not be permitted to leave your room until Day 14.

During your stay in the quarantine unit, you will not be able to socialise with anyone else and will have contact only with the study team. You are welcome to bring your mobile phone and laptop, and watch TV and films, but you cannot have any visitors. There will be Wi-Fi. Your room will have its own en-suite bathroom.

There will be no cooking facilities; meals will be provided by staff. You will receive 3 meals per day and snacks will also be provided. All dietary requirements are catered for, including vegetarian, vegan, halal, kosher and gluten free. You will have a small fridge and a kettle in your room. You can bring snacks in with you when you are admitted to the quarantine unit. The study staff will ask that you don't have any caffeinated drinks such as coffee within 30 minutes of your observations (blood pressure and heart rate) being collected.

While you are with us, you will have blood tests, swabs of the nose and other procedures every day. Most of the daily research samples will be collected in the morning and some in the afternoon. You will have your vital signs collected four times throughout the day. The study team will aim to complete the interventions prior to 9pm and will not disturb you during the night. The procedures that will be done during quarantine are detailed in Appendix 1.

You will be asked to complete a symptom diary three times a day during the quarantine and also complete some cognitive tests and smell tests.

It is important that you stay in the unit until the study team discharges you. We want to be sure that if you get symptoms of COVID-19 infection, we can monitor you and give you treatment if necessary. We also want to be sure that you cannot spread COVID-19 to other people. You need to be available and willing to stay in the unit for at least 2-3 weeks. You should make plans for childcare needs or emergencies that may occur during the study.

Once discharged, please contact the study team immediately if you:

- **Receive a COVID-19 vaccine or think you may have caught COVID-19**
- **Receive any medical care outside of the study (GP or hospital attendances)**

Reserve Participants

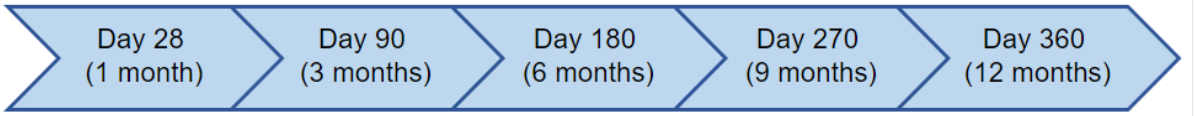
We may invite extra participants to the quarantine part of the study in case another participant becomes ineligible to take part between admission day and being infected on Day 0. The study team may invite you to be a reserve participant. If you agree, you will be invited to the quarantine unit on the same day as the other participants and will be staying in one of the rooms in the quarantine unit. You will undergo the same study procedures on Day -2 and Day -1 as the other participants (see Appendix 1.).

Should one of the other participants no longer be taking part, you will then continue in the study and be infected on Day 0 and stay for a further 10-14 days in the quarantine unit. Should none of the other participants drop out, you will be discharged and invited for the next quarantine group, or the next convenient quarantine based on your availability, as a main participant rather than a reserve.

If you agree to be a reserve participant for the quarantine part of the study, you will be paid for the time you spend in the quarantine unit at £200 per day.

5.1.5 Follow Up

Following discharge from the Quarantine Unit, you will be telephoned a week later, on Study Day 21, to check your health and if you have had any health issues since being discharged. You will be asked to return for clinic visits at the CCVTM/ Oxford EMCRF at the following times after discharge from the Quarantine Unit, so we can monitor your health after the infection:



The follow up visits will include blood and urine samples, nose and/or throat swabs, vital signs, physical exam, cognitive tests, smell tests and other assessments and procedures as detailed in Table 1 and Appendix 1.

For each scheduled follow-up visit you attend, you will be paid £200 per visit.

5.1.6 COVID-19 Testing Visits

Following discharge from the Quarantine Unit, you will be given lateral flow tests and/or PCR swabs to take home with you. If you develop any symptoms of COVID-19, you will need to contact the study team on the phone number provided so they can assess whether you need to perform a self-swab. If the lateral flow test indicates a positive result, the study team may ask you to perform a further swab for a PCR test and may ask you to attend the CCVTM/ Oxford EMCRF for a COVID-19 testing visit within 7 days of your symptoms beginning. If this

is not possible, they may try to arrange a home visit with you if you agree to this and the study team are able to do so.

If you are required to perform lateral flow or PCR tests for work, attending events or travelling abroad, please do not use the kits provided by for the study. If you do have to do a test for any other reason and your result comes back positive, please inform the study team straight away on the phone number or email provided. Again, they may ask you to perform a further swab for a PCT test or to attend the CCVTM/ Oxford EMCRF or arrange a home visit for a COVID-19 testing visit within 7 days of your symptoms beginning (or positive test if you do not have symptoms).

If you do come in for a COVID-19 testing visit, the study team will ask you about your symptoms and any medication you have taken. They will take some swabs and blood samples. They may also check your vital signs such as blood pressure and oxygen saturation, as well as perform a directed physical examination if indicated.

You may also be invited for a second COVID-19 testing visit around 28 days after the first COVID-19 testing visit. The same assessments and samples will be taken as mentioned above for the first COVID-19 testing visit.
If you attend an onsite COVID-19 testing visit, you will be paid £100 per visit.

5.2 What tests and procedures will I have during the study?

During the study, we will look after you at all times and monitor your health as necessary. If the doctor wants to confirm a test result, he/she may ask you to have an extra test.

Tests/Procedures	
Documents	
Informed Consent Form	You will be given an informed consent form to read and sign before any study procedures are performed.
Symptom Diary Card	During Quarantine, you will be given a symptom diary card to complete 3 times a day (either on paper or electronically) which asks you questions about how you are feeling and any cold-like symptoms you may have.
Cognitive Tests	Using an app called “CogAssess” on a tablet that we provide, you will complete some tests of your reaction time and other brain functions as well as questionnaires on the quality of your sleep. The tests will take around 20-30mins to complete.
Health Questionnaires	You may be given two short questionnaires. The Patient Health Questionnaire (PHQ-9) and the Generalised Anxiety Disorder Questionnaire (GAD-7).
Measurements/Scans	
Height and weight	You will be asked to remove your shoes and then stand against a height stick to record your height. You will also be asked to stand on scales to record your weight.
Vital Signs	We will measure your heart rate, breathing rate, blood pressure, oxygen saturation and temperature). Using an observation machine, we will place a cuff around your arm that will inflate and then deflate to measure your blood pressure, a small device will be clipped onto your finger to check the amount of oxygen in your blood, and it will also tell us your heart rate. A study doctor/nurse will measure your breathing rate by watching your chest expand as you inhale. A temperature probe will be given to you to place under your tongue to measure your temperature.
Physical Examination	A study doctor will look at your skin, listen to your chest, feel your abdomen, look in your mouth and feel the lymph nodes in your upper body (around your neck and in your armpits).
Chest X-Ray	This is performed once at the screening visit and is a safe and painless test that uses a small amount of ionising radiation to take a picture of your chest and lungs. You will be provided with a hospital gown to change into and asked to lie down or sit up for a short while during the scan.
Electrocardiogram (ECG)	This looks at your heart’s activity. It is a painless procedure where small pads will be stuck to your arms, legs and chest (which may need to be shaved) while you lie still for

	a few minutes. You will be required to undress to the waist. The pads can sometimes cause minor skin irritation.
	Spirometry is a type of lung function test. It is either a small machine attached by cable to a mouthpiece or a handheld device with a mouthpiece. You will take the deepest breath you can, then exhale long and hard into a tube. This can make you cough or feel short of breath for a short time.
UPSIT Test	The University of Pennsylvania Smell Identification Test (UPSIT) is a test used to assess your sense of smell. A booklet will be given to you which you will work through to "scratch and sniff" various odours and identify them. You will be scored on how many smells you correctly identify out of 40. We will record a baseline smell score before giving you the virus and then ask you to do the UPSIT test to check for changes in your sense of smell during the study.
Vascular measurements	This may only be performed on some participants depending on what cohort they are in and which study site they are participating at. You will be informed whether you will be having these measurements performed or not. Whilst lying down, a blood pressure cuff will be placed around your arm and probes will be placed on your fingers. The blood pressure cuff will be inflated for 5mins and then deflated for 5mins.
Samples	
Urine test	You will be asked to provide a urine sample to test for infection, ill health, drugs of abuse, nicotine (from smoking), and pregnancy (for women of child-bearing potential only).
Nasal sampling	Nasal swabs will be obtained by placing a swab into your nostrils. Swabs may be taken from the middle or back of the nose. Nasal fluid will be obtained by placing a nasosorption strip inside your nostril for 2 minutes. This strip is flexible and absorptive like filter paper. Nasal cells may be obtained by a member of the study staff using a tiny plastic scoop that goes into your nose about 3cm up to collect cells. These nasal sampling procedures are not painful and do not require local anaesthetics. They may cause minor discomfort for a few seconds, and can cause a small nosebleed, make you sneeze, and/or temporarily leave you with watery eyes and a runny nose. The study team will monitor your nose for any irritation and the samples will be collected from alternate nostrils.
Throat swabs	We will ask you to tilt your head back and open your mouth while a swab is rubbed along the back of your throat. You will need to resist gagging and closing your mouth.
Lateral Flow Tests	You will be provided with a lateral flow antigen test and asked to the test yourself following the manufacturer's instructions. Once performed, the lateral flow test will be immediately removed by study staff so you cannot read the result.
Saliva Samples	You will be asked to provide a saliva sample in a container of around 2mls.
Dried Blood Spot (DBS) Finger prick capillary sample	This is optional. A small lancet will be used to prick the end of your finger. Your finger will be squeezed by a member of the study team to collect a few drops of blood on a card. Your finger may be a little sore for a short while after this. This sample will then be sent to the UK Health Security Agency for analysis as part of their ongoing research projects. They will not be sent any personally identifiable information about you. They will receive the sample with a study ID number only, and may want details about your age, gender, COVID-19 vaccination and infection history.
Blood Samples	We will take blood to test for: • Anaemia (low red blood cells) or problems with your immune system • Blood clotting problems • Liver, kidney, thyroid and heart function • HIV, Hepatitis B and Hepatitis C infection • Diabetes or impaired blood sugar control

	• HLA type (this tells us the types of proteins or "markers" on your cells, and will only be performed if you consent to genetic analysis) • SARS-CoV-2 antibodies (to check for evidence of infection and vaccination). We will take between one teaspoon and 5 tablespoons each time. The total amount of blood we collect will not exceed 550ml over 8 weeks (the same amount taken at a blood donation session), unless for safety reasons when additional samples may be required. So that you don't give too much blood, you should not donate blood from the time of the Screening visit until 3 months after the last study visit. You may feel dizzy when you have blood taken. Sitting or lying down when blood is taken should stop you feeling lightheaded or fainting.
Stool swab samples	You will be asked to collect a stool swab by rubbing a cotton-headed swab on used toilet paper after opening your bowels during the quarantine stay only.
Environment Sampling	This may only be performed on some participants depending which study site they are participating at. You will be informed whether you will be having these samples taken or not. During quarantine, we will enter your room up to two times a day to take samples from the air and surfaces to see if the virus stays in the environment.
Mask-wearing samples	This may only be performed on some participants depending which study site they are participating at. You will be informed whether you will be having these samples taken or not. You will be asked to wear a single use face mask for 30-60mins once or twice a day for us to take samples and study the levels of the virus that are present in your breath. s
Breath aerosol sampling	This may only be performed on some participants depending on what cohort they are in and which study site they are participating at. You will be informed whether you will be having these samples taken or not. You will be asked to breathe into a mouthpiece or via a face mask which has tubing attached to a machine that can measure the aerosols you expire. This will take around 15 mins and you may be asked to talk, cough or exhale deeply during this test.

Table 1. Tests and Procedures performed during the study

5.2.1 What happens if something unexpected turns up during my tests?

If we find any health abnormalities during the study, we will inform you and, if necessary and with your consent, we will inform your GP and refer you to a specialist.

5.2.2 Are you looking at my genes?

Blood samples contain genetic information in the form of DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). DNA contains the genetic 'instructions' for the ways the various parts of your body work. This information can also be obtained from a process called 'sequencing' of your RNA.

Differences in these genetic 'instructions' between individuals may help to explain why some people are more likely to get a particular disease, why some people become sicker than others, and why some medications work better for certain people. The sponsor would like to study your genetic information in the blood samples that will be collected from you during the study to improve its knowledge of how the study virus affects the human body in the disease process. As medical and scientific knowledge develops, samples we collect now could be invaluable to future research.

Some of the blood and nose samples we collect can be used to look at your genes. The genes we will be looking at are those which are involved in protecting us from infections. This will involve looking at genes that are turned on and off during infection with COVID-19 virus and whether the patterns of these are linked to the likelihood of developing symptoms. In addition,

we may look at your DNA sequence directly to see if there are inherited differences that influence risk of infection.

Please note that your genetic information will not be used for your medical care. The test results cannot be used to make a diagnosis of your health, and neither you nor the study doctor will be given specific information about the results.

5.2.2.1 Do I have to have genetic testing of my samples?

No, you do not have to. Agreeing to the genetic testing of your samples is completely optional and if you do not consent to genetic testing of your samples, you will still be able to continue in the study. Your decision will not affect the care that you will get from the study doctor.

If you do consent to genetic testing, you can change your mind at any time and withdraw your consent. This will not affect the compensation you are entitled to receive as a result of taking part in the study.

If you wish to withdraw your consent, please notify the study doctor. If you withdraw your consent to genetic testing of your samples, genetic testing will not be done. A record of your signed consent and your withdrawal would be kept as evidence of your wishes.

5.2.2.2 What are the costs and benefits of agreeing to genetic testing of your samples?

There will be no cost to you, and no direct benefit to you from agreeing to the genetic testing of your samples. You will not be paid for these samples or tests, and the sponsor will not offer you any payment as a result of any development or commercial sale of any product created as a result of this or any future studies.

5.2.2.3 Samples for genetic testing

If you consent to this, samples collected during the study will be used genetic testing. If you consent to provide additional samples to be used for genetic testing, these samples will be collected during the quarantine part of the study. We usually take blood sample(s) for genetic testing at the same time as a scheduled blood test in the study, so an additional needle prick is not usually necessary.

The samples collected for genetic testing may not be tested immediately and the exact nature of the tests that will be done is not known at present but could include sequencing or investigation of specific mutations (changes to your DNA). Any testing will be subject to ethical review as appropriate.

5.3 What are my responsibilities if I agree to enter the study?

We have a code of practice to protect participants' well-being and to safeguard the outcome of the study. If you do not respect the code of practice, it can affect the quality of the data collected and compromise yours and the study team's safety, such that, depending upon the situation, we may have to reduce your compensation. This would be at the discretion of the trial Sponsor, Imperial College London, following discussions with the site Principal Investigator and the participant responsible.

We ask that you

Please:

- ✓ answer questions about your medical history honestly and completely
- ✓ tell the study staff if you take any medicines or treatments (e.g., tablets, sprays, creams, medicines, and inhalers, including over the counter medications, multivitamins, homeopathic and herbal medicines). You will be told which medications are and are not allowed during the study.
- ✓ follow the requirements for contraception during the study (see Section 3.1.5).

- ✓ treat members of staff and other participants with courtesy and respect
- ✓ comply with the study restrictions and any instructions given to you by study staff
- ✓ be punctual for your daily appointments and respect staff coming into your room to take assessments during the quarantine period
- ✓ respect confidentiality
- ✓ keep your room in the in-patient quarantine tidy
- ✓ take care with property and equipment at the study sites
- ✓ tell the study staff immediately of any changes in symptoms or health and well-being including if you develop any COVID-19 symptoms or have any positive tests for COVID-19 (PCR or lateral flow) during the study.
- ✓ show consideration to other participants and study staff by limiting excessive noise such as playing loud music

Please do not:

- × withhold significant medical information at any point during the study
- × donate blood during the 12-month study or take part in any other studies that involve blood sampling or the administration of drugs or vaccines.
- × have any live vaccines 60 days before you come into the quarantine unit nor any inactivated vaccines 30 days before you come into the quarantine unit. Please check with the study team if you have any vaccines planned or are unsure what vaccines you can and can't receive and when.
- × donate any sperm/an egg for at least 6 months after being given the study virus
- × take part if you are currently breastfeeding, pregnant, or have been pregnant within the past 6 months prior to being given the study virus
- × take any hay fever medication for 7 days prior to being given the study virus
- × smoke, vape or use any nicotine containing products during the quarantine period. We will test for nicotine prior to giving you the study virus.
- × drink alcohol during the quarantine stay or within 3 days of a scheduled study visit
- × use recreational drugs at any point during the study from the screening visit until the last follow up visit at day 360.
- × bring medications into quarantine without our prior consent
- × take any medicines other than those given to you by the study staff during the quarantine period
- × be late for daily appointments / temperature recordings / study procedures
- × behave inappropriately (e.g., be rude or uncooperative)
- × leave the quarantine unit without being discharged by a study doctor
- × agree to take part in this study if you cannot commit to staying in the quarantine unit for entire time planned or if you cannot commit to attending all the follow-up visits
- × take photographs and/or video recordings during the quarantine visit or at any study visit

Internet use during the quarantine stay

Before you use the internet connection provided for the study, please be aware that:

- Internet use is monitored by the hospital IT team
- Illegal downloading or sharing of copyrighted material (music, films, and TV shows etc) is prohibited
- Accessing inappropriate, pornographic, illegal file sharing and streaming sites is prohibited
- The equipment that you bring into the quarantine unit may need to be tested for safety prior to you being able to use it (this includes for example a phone charger)

Please feel free to use legal media sites for example:

- ✓ Netflix / Amazon Prime / Disney+ / BBC iPlayer / ITV Player
- ✓ Spotify / Apple Music

Please note that if you agree to take part in this study, you will be asked to sign an informed consent form which states that you have read and understood the information from this participant information sheet. By signing this, you are agreeing that you have read and will adhere to the rules and guidelines mentioned in this section (Section 4.3).

5.4 What happens when the research study stops?

Your time in the study will end once you have completed your final follow up visit at 12 months post viral challenge. You will not need to do anything further. You will be thanked and reimbursed for your time and expense.

If you require any extra follow up with the study team after your 12-month visit for the purpose of the study, this will be discussed with you. If you require any extra follow up with your GP or specialist after the study, we will write to them to let them know you have completed the study and they need to arrange a follow up with you.

5.4.1 Could my participation end early?

Yes, your participation in the study could end early. At no point can we guarantee that you will complete the study.

The Sponsor (Imperial College London) or the regulatory authorities can stop the study at any time. Additionally, the study doctors could decide to take you out of the study at any point if they think it is necessary, as outlined below.

Throughout the Screening process, up to the point of administering the study virus, we will be collecting information about your health, including from your GP and the screening tests. Sometimes, we identify reasons that may make us decide that it is not in your best interest to take part in the study. This decision would be made by the study doctors and is made to protect your well-being.

Sometimes we invite more participants to a study than are required as reserve participants, in case some are no longer suitable for the study. We will ask if you are happy to be a reserve participant and inform you when this may be the case so you can plan accordingly. If you are not required to participate further, you will be paid for your time up to that point. You may be able to join another quarantine group or study if it is appropriate.

If you do not cooperate, or, in our reasonable opinion, comply with the study procedures, you may be taken out of the study by the study team, which could lessen the amount of compensation you receive.

If you withdraw from the study, you will be asked to sign a form telling us how you would like us to use your study samples and information. You may also ask the study team to remove your personal details (e.g., address and date of birth) from its participant database. However please note, that any of your data which has been recorded in the clinical trial would not be withdrawn or erased from the study so that we can still meet our legal obligations and to maintain the scientific integrity of the study. A record of your decision would be kept.

5.5 What expenses and compensation will I receive for being in the study?

You will be paid for your participation in the study as follows:

Visit	Amount
Pre-Screening Visit	Not paid.
Screening Visit	£70
Quarantine Stay	£3,400 (£200 per day)

Extra Quarantine Days (if applicable)	£200 per day
Day 28 Visit	£200
Day 90 Visit	£200
Day 180 Visit	£200
Day 270 Visit	£200
Day 360 Visit	£200
COVID-19 Testing Visit 1 (if applicable)	£100
COVID-19 Testing Visit 2 (if applicable)	£100
TOTAL (minimum received)	**£4,470**

Table 2. Participant Payment breakdown by visit

Please note, if you are discharged from the quarantine unit on Day 10 because you remained uninfected, you will be asked to attend study days 11, 12, 13 and 14 at the Oxford EMCRF for sampling and assessments. You will receive £200 a day for attending those visits and therefore will receive the same as the participants required to stay in the quarantine unit until Day 14.

Milestone	Amount
Paid shortly after attending a screening visit	£70
Paid shortly after discharge from quarantine	£1,700 *(plus any additional days stayed in quarantine at £200 per day, if applicable)*
Paid shortly after the Day 90 visit	£400
Paid shortly after the Day 180 visit	£200
Paid shortly after the Day 270 visit	£200
Paid shortly after the Day 360 visit	£1,900
Total	**£4,470**
Paid shortly after the COVID-19 testing visit *(if applicable)*	£100
Paid shortly after discharged from quarantine as a reserve participant ***(if applicable)***	£200 per day

Table 3. Milestones for receiving payments

Additional visits or expenses:

- You will not be additionally reimbursed for travel expenses to and from the quarantine unit or from the scheduled study visits. However, at the study team's discretion, reasonable travel expenses to unscheduled visits, such as to attend a COVID-19 testing visit or due to staying extra days in the quarantine unit, may be reimbursed but must be agreed prior to the cost being incurred by the participant. If it is agreed by the study team to be reimbursed, receipts must be provided.
- At the study team's discretion, reimbursement of any additional cost incurred by the participants (for example private medical appointments, etc.) must be agreed with the study team prior to the cost being incurred by the participant. If it is agreed by the study team to be reimbursed, receipts must be provided.

Payment in the event of withdrawal or exclusion:

- If you do not complete the study (for example if you withdraw your consent, are excluded, or are considered as a reserve participant) you will receive payment in line with the visits you attend (and the time you spend in the quarantine unit if applicable).

We will not pay tax or National Insurance from the money due to you. It is your responsibility to pay these and to check how any compensation received from taking part in the study affects any state benefits to which you are entitled. Contact HM Revenue & Customs for information

(http://www.hmrc.gov.uk/ or telephone 0300 200 3300). Please note that there are some situations where we are required to tell the authorities about your payments if we are asked to.

Please initial this box to confirm you have read and understood **Section 5**	

6. What are the health benefits of taking part?

Taking part will not improve your health, although you may benefit from a general health check. We hope that this study will support the development of more COVID-19 vaccines/treatments that could help many people around the world. There is a chance you could develop "immunity" against COVID-19, but we don't know if you will or for how long protection might last.

7. LEGAL INFORMATION

7.1 What if I want to withdraw from the study?

You are free to withdraw from the study at any time you wish, however If you decide to withdraw your consent and "leave the study" during the quarantine phase, you will be very strongly encouraged to remain in the quarantine unit until you are no longer contagious. This is for both your safety and that of others whom you could infect as a contact. In this situation, we would continue to optionally offer you all procedures considered important for safety purposes by the study team but would stop any research procedures. This would include:

- Regular vital signs
- Medical review of any symptoms
- Safety blood tests (but not research ones)
- Rescue therapy (if being offered)

Remaining in the unit would therefore allow close follow-up by the study team and receipt of the rescue therapy. If you have to leave the quarantine unit before you have been formally discharged, you must self-isolate at home and avoid contact with anyone else until the discharge date (14 days after you were given the virus) as you will have been exposed to a strain of SARS-CoV-2 that is not widely circulating any more to avoid the possibility of causing an outbreak.

In the event that you decide to leave the unit early:

- You will be strongly advised to self-isolate at home until you are no longer infectious and given advice about hand-washing and other infection control measures.
- You should be collected from the quarantine unit in a private vehicle by a family member or friend so you do not expose the wider public to the virus. You should inform them of their risks of getting infected by you and we would recommend that you both wear a facemask for the journey home.
- If you return home and there are other people in your household, they should be strongly advised to self-isolate for 14 days after you return home; this will be explained to you before you leave.
- You may not be eligible to receive the rescue therapy (if being offered) if you leave quarantine before the planned date of treatment.
- With your agreement, you will be contacted daily by the study staff (i.e. study doctor or nurse) via phone call to check on your health and to remind you of any self-isolation recommendations until the study doctors are satisfied that daily follow up can end. If possible, the study team may also visit you at home and perform swabs to check if you are still infectious.
- The local health protection team may be informed of your return home and may contact you

If you withdraw from the study, we will keep and use information about you that we already have because some research using your data may have already taken place and this cannot be undone.

7.2 What if something goes wrong?

You must tell the study staff immediately if you have any health problems during the study. You will be given an emergency contact card when you are discharged from quarantine, which provides a 24-hour telephone service in case you need to contact us outside of office hours. If you need to attend another doctor for health problems relating to the study, we will ask that doctor to provide details that will help us follow up your care and investigate the possible reasons for these health problems.

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the investigator, Professor Chris Chiu (c.chiu@imperial.ac.uk). The normal National Health Service mechanisms (https://www.nhs.uk/using-the-nhs/about-the-nhs/how-to-complain-to-the-nhs/) are also available to you. If you are still not satisfied with the response, you may contact the Imperial College Research Governance and Integrity Team (https://www.imperial.ac.uk/research-and-innovation/research-office/research-governance-and-integrity/).

7.3 Who has reviewed this study?

The Specialist Ad hoc Research Ethics Committee (REC) have looked at the details of this study and have given it a Favourable Opinion. This is an independent group of experts and non-experts set up by the NHS Health Research Authority to review the ethics of this research.

7.4 Research study registry

A description of this study will be available on a clinical trials database e.g., www.clinicaltrialsregister.eu or http://www.ClinicalTrials.gov . This will not include information that could identify you. At most, the website will include a summary of the results. You can access the results of the study by visiting either website and searching for the study details included in this participant information sheet approximately one year after the trial has ended.

7.5 Who is organising and funding the research?

This research is funded by the Wellcome Trust and is being sponsored by Imperial College London and conducted by The University of Oxford.

Please initial this box to confirm you have read and understood **Section 6 and 7**	

8. KEEPING YOUR DATA SAFE

8.1 How will we use information about you?

This next section describes how we will keep your data safe. In summary, it says that all parties involved in this study will treat your data in accordance with the law and best practise. Access to your personal data will be strictly limited to those who need it and will be kept strictly confidential. Your biological samples will be stored in secure locations with labels that cannot directly identify you and will be destroyed 25 years after the study finishes unless you consent to their future use.

8.1.1 Data Protection and Privacy

All research samples that go to the sponsor (Imperial College London), or other collaborators, will be labelled only with your participant I.D. number. This means your personal data is partly anonymised (pseudonymised), so that those who get access to your samples cannot identify you. The only people who can link your I.D. number to you are doctors, nurses and other members of the study team who are working directly with you.

There are some samples, such as bloods and swabs which are analysed by the NHS labs and ordered via the local hospitals electronic patient record (EPR) system. As these are ordered and processed within the Hospital system, they will be linked to your personal hospital record and so can be linked to you. Your hospital record and the NHS Lab bloods and swabs, will not have your participant I.D number on. Only the study team will hold both elements of information.

Any physical documents containing your personal information will be stored securely in a locked cupboard in a restricted access location that only delegated members of the study team can access, Your personal data will also be held securely on a database, treated in strictest confidence and will be held in accordance with data protection legislation. Access to personal information will be limited to authorised staff within Imperial College London, The University of Oxford and regulatory authorities such as the HRA. These organisations have a duty of confidentiality to you as a potential research participant.

Your records and personal information will be treated in the strictest confidence. You have right of access to any personal data being held by the study team. In the event of any inaccuracies recorded in the data, you have the right to request that such data be corrected. Please contact your study team using the contact details which you have been provided if you would like to view any of the personal data which is held about you or make use of any other right that you may have under applicable data protection laws.

Imperial College London is the sponsor for this study and will act as the data controller for this study and the participating study sites will act as data processors. This means that we are all responsible for looking after your information and using it properly. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

This study is stated to finish in December 2024.

We will need to use information from you, your medical records and your GP for this research project. This information will include your name, NHS number, contact details and medical history.

We will also collect your passport number or National Insurance number in order to register you on The Over-Volunteering Protection System (TOPS). You can find out more about TOPS here: https://www.hra.nhs.uk/about-us/committees-and-services/the-over-volunteering-prevention-system/

We will also collect your bank details so that we may pay you for your participation in the study.

People within the study team (see section sharing your information with others) will use this information to do the research or to check your records to make sure that research is being done properly and the information held (such as contact) details is accurate.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

• Imperial College London - “performance of a task carried out in the public interest”); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies on scientific or historical research purposes or statistical purposes.

8.1.2 International Transfers

There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA. Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your personal data is processed.

8.1.3 Sharing your information with others

We will only share your personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.
Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third-party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.
The following Research Collaborators / Partners in the study.

- University of Oxford

8.1.4 Potential use of study data for future research

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this

country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

8.1.5 Commercialisation

Samples / data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure that your name and any identifying details will NOT be given to these third parties, instead you will be identified by a unique study number with any sample / data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be created using your data (in a way which does not identify you individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your data will not be shared with a commercial organisation for marketing purposes.

8.1.6 What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep and use information about you that we already have because some research using your data may have already taken place and this cannot be undone.

- If you choose to stop taking part in the study, we would like to continue collecting information about your health from you. If you do not want this to happen, tell us and we will stop.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we already hold about you if this could affect the wider study or the accuracy of data collected.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

8.1.7 Storage and use of samples and information from this study

The Sponsor and/or University of Oxford will keep all the biological samples and related data collected from you during the study to allow us to fully study and understand the disease. The Sponsor and/or University of Oxford will send your biological samples for testing in laboratories where they will be stored securely until the end of the study.

Your biological samples will be kept for a maximum of 25 years from the end of the entire study. After this time, the samples will be destroyed. Your biological samples will be labelled with your study participant number but we will not use your name or information that could identify you.

As mentioned above, there are some samples, such as bloods and swabs which are analysed by the NHS labs and ordered via the local hospitals electronic patient record (EPR) system. As these are ordered and processed within the Hospital system, they will be linked to your personal hospital record and so can be linked to you. Your hospital record and the NHS Lab bloods and swabs, will not have your participant I.D number on. Only the study team will hold both elements of information.

At the end of the study, some of your leftover biological samples and data from this study could be useful for other health research and laboratory testing. You will be invited to consent to storage of your samples for future use in other ethically approved studies. Any movement and storage of biological samples will be in accordance with the Human Tissue Act 2004 and other relevant laws in the countries they are sent to. You would not be told the results of such other research. You can still take part in the study if you do not want your leftover samples and information to be stored for future research.

Additional research may include genetic testing of the samples, for example to examine genes related to the immune system that may be involved in the response to COVID-19. You will be invited to consent to the use of your samples for genetic testing. You can still take part in the study if you do not want genetic testing to be carried out on your samples.

8.1.8 Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the study team
- by sending an email to Covid19-challenge@paediatrics.ox.ac.uk
- by ringing us on 01865 611 424/ 07990431010
- by going to our website pages https://trials.ovg.ox.ac.uk/trials/covhic002

8.2 Complaints

If you wish to raise a complaint on how we have handled your personal data, please contact the study team first by sending an email to Covid19-challenge@paediatrics.ox.ac.uk or by ringing us on 01865 611 424/ 07990431010.

Following our response, if you are not satisfied please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk , via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you remain unsatisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO)- via www.ico.org.uk. Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

8.3 What will happen to the results of the study?

If any results or publications are made publicly available during your participation in the trial, the study team will inform you where you can read these or provide you with a copy. If any results or publications are made publicly available after you have completed the trial, information about these can be found on the https://trials.ovg.ox.ac.uk/trials/covhic002 . You will not be identified in any report/publication.

There is also an optional statement on the consent form for you to agree to the study team contacting you after you have completed the study to send you relevant publications.

Please initial this box to confirm you have read and understood **Section 8**	

9. Media

We may ask to take photos and/or videos of you during the study. This media could be used in press releases, news articles, to promote the study on our website and social media platforms, and also for training purposes. You may be identifiable in these images and videos.

Agreeing to this is completely optional and if you do not consent, you will still be able to continue in the study. Your decision will not affect the care that you will get from the study doctor. If you do consent to this, any photos or videos that are taken will be securely stored.

If you do consent to this, you can change your mind at any time and withdraw your consent. If you wish to withdraw your consent, please notify the study doctor.

If you withdraw your consent, we may not be able to remove images of you that are already public but we can ensure they are not used going forward and we will not take any new images or videos of you.

10. Contact for further information

If you have any questions about taking part in this research study, please contact the study team:

Principal Investigator: Professor Helen McShane
Email: Covid19-challenge@paediatrics.ox.ac.uk
Phone: 01865 611 424

If it is an emergency, please use the telephone number provided to you on the Emergency Contact Card to contact the study doctor as soon as you can.

Now that you have read this participant information sheet and a study team member has gone through it with you in detail, there will be a break. Please take the opportunity to make sure everything is clear to you and ask as many questions as you want. To help check that we have given you all the key information, you will be asked to complete the Multiple-Choice Questionnaire prior to signing the consent form.

11. APPENDICES

11.1 APPENDIX 1. Schedule of Study Activities

Study Day	Pre-screening	Screening	Day -2	Day -1	D0 Challenge	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Extended Days in Quarantine (if applicable)	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal	COVID-19 Testing V1 (as required)	COVID-19 Testing V2 (28 days after COVID-19
Written informed consent	X	X																										
Medical & medication history		X																										
Height & weight		X	X																									
Urine samples		X	X						X			X			X				X		X	X	X	X	X	X		
Urine pregnancy test		X			X																							
Blood samples	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Physical examination		X	X		(X)	(X)	(X)	(X)	X	(X)	(X)	X	(X)	(X)	X	(X)	(X)	(X)	X	(X)	X	X	X	X	X	X	(X)	(X)
Vital signs and temperature		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Symptom diary cards			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Smell Test (UPSIT)				X		X			X			X			X			X		(X)	X	X	X	X	X			
Cognitive Tests				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X			
Chest X-ray		X																										
12-lead ECG		X	X		X	(X)	(X)	(X)	X	(X)	(X)	X	(X)	(X)	X	(X)	(X)	(X)	X	(X)	X	X	X	X	X	X		

Study Day	Pre-screening	Screening	Day -2	Day -1	D0 Challenge	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Extended Days in Quarantine	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal	COVID-19 Testing Visit 1 (as required)	COVID-19 Testing Visit 2 (28 days after COVID-
Spirometry		X	(X)			(X)	(X)	(X)	X	(X)	(X)	X	(X)	(X)	X	(X)	(X)	(X)	X	(X)	X	X	X	X	X	X		
Challenge Virus inoculation					X																							
Nose and throat swabs		X	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)	(X)	(X)			X	X	X
Nasal curettage and/or nasopharyngeal swab		X	X			X		X		X		X			X				X		(X)							
Saliva sample		X	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)					X		
Self-performed lateral flow test			X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X								
Nasosorption strips		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Mask wearing sampling			X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)	(X)							
Only for some participants. Breath aerosol sampling			X					X				X			X				X		(X)							
Environmental viral sampling			X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)								
Only for some participants. Vascular measurements (EndoPAT)			X					X				X			X				X									
Stool swabs			X			X	X	X	X	X	X	X	X	X	X	X	X	X	X									

Key:
X = occurs on this day at least once per day/visit
(X) = is either optional to participants or occurs at the investigators discretion

10.2 APPENDIX 2. Optional Assessments and Procedures Schedule of Study Activities

Study Day	Pre-screening	Screening	Day -2	Day -1	D0 Challenge	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Extended Days in Quarantine	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal	COVID-19 Testing Visit 1 (as required)	COVID-19 Testing Visit 2 (28 days after COVID-19 Testing V1) +/- 7 days
Optional Assessments and Procedures																												
Patient Health Questionnaire (PHQ-9)		X	(X)												(X)				(X)	(X)								
Generalised Anxiety Disorder Questionnaire (GAD-7)		X	(X)												(X)				(X)	(X)								
Dried blood spot (finger prick)	(X)																				(X)	(X)	(X)	(X)	(X)			

Key:
X = occurs on this day at least once per day/visit.
(X) = is either optional to participants or occurs at the investigators discretion

Note: the PHQ-9 and GAD-7 questionnaires will be completed by all participants who undergo screening. The investigator may then decide to repeat these questionnaires at the Day -2/-1, Day 10 or Day 14 visits and for any extended stay days in quarantine.
Note: the dried blood spot sample is completely optional to participants.