



CONVALESCENCE study

Participant Information Sheet

(Ethics ref: 21/SC/0235)

Chief Investigator: Professor Nishi Chaturvedi

We would like to invite you to take part in the CONVALESCENCE study (**CO**ro**Na**Virus post**A**cute **L**ong-term **E**ffect**S**: **C**onstructing an **E**vid**E**N**C**E base) which explores the long-term effects of COVID-19 and the mechanisms that determine the consequences of these outcomes.

This information sheet tells you more about the study and explains what will happen if you decide to take part. Please take your time to read this information sheet and ask any questions you may have.

COVID-19 National Core Study



Coronavirus post-acute long-term effects: constructing an evidence base

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What is the purpose of the study?

The aim of this project is to better understand why some people experience difficulty returning to normal health following COVID-19 infection with novel coronavirus-2 (CoV-2) - a condition often called 'long COVID'. The findings will help define, diagnose and describe long COVID. They will also help us to identify what risk factors are linked to a person's likelihood of developing long COVID. We hope this research will lead to a better understanding of the mechanisms of long COVID and point to ways that we can enhance recovery, improve healthcare, and assist people back to full health more quickly.

Why have we approached you?

This project involves participants from a number of cohort studies across the UK. You are a member of the TwinsUK cohort and based on their records you appear to be eligible to participate in this study.

Do you have to take part?

No, it is up to you to decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What happens if you take part?

You will be invited to attend a research clinic at the Bloomsbury Centre for Clinical Phenotyping (BCCP), in the Institute of Cardiovascular Sciences at UCL for approximately 3-4 hours, including breaks. We will reimburse reasonable expenses for travel to and from the clinic and cover the cost of hotel accommodation, if necessary.

We understand that some participants may like to bring along a traveling companion or someone to act as a consultee (someone who acts as a trusted adviser to help with any aspect of the research, for example a spouse or other next of kin). We would also pay for their expenses.

You will also be invited to wear an activity watch and download an app to your mobile phone.

What measurements will you have performed?

The measurements described below are included in the study. We may not invite you to participate in all these tests and will only invite you to participate in tests that are safe for you.

Questionnaires

We will ask you some questions about your general health and any medications you may be taking.

Body composition, blood pressure, electrocardiogram (ECG), eye imaging, muscle function, balance, and blood and urine sample

We will measure your height, weight and percentage fat (using special scales). We will also measure your waist and hip circumferences using a tape measure.

We will measure your heart rhythm using an electrocardiogram (ECG). We will ask you to lie on a couch on your back and attach sticky electrodes to your limbs and across your chest on the left side of your body. We will ask you to relax for 5 minutes while we make recordings.

We will measure your blood pressure lying, sitting and standing using a blood pressure monitor which inflates a cuff around your upper arm.

We will take pictures of the small blood vessels in your eye using a special camera (optical coherence tomography (OCT) imaging). This is similar to the methods used at the optician, it is very safe and does not require eye drops. With your permission, we will store these images (using an anonymous identification code) in a secure electronic database for future analysis. You will not be identifiable from these images. Hand-grip strength will be measured with a hand-grip dynamometer which consists of a gripping handle and a digital display. We will also ask you to do a standing balance test, a walking speed test over a 3 meter distance and 5 sitting to standing chair rises.

We will take a non-fasting blood sample (no more than 30ml which is approximately 6 teaspoons); a fine needle is used to take the blood sample. We will also provide you with a collection pot and instructions for a urine collection (10ml). Some of blood and urine will be analysed during the clinic visit and some will be stored for analysis later.

Lung function, echocardiography and exercise testing

We will assess your heart function using echocardiography. To do this we will ask you to lie on your left side and ultrasound gel will be used on your skin over the chest area. This is not harmful but may be a bit cold. A probe placed on your chest will image your heart beating on the monitor (center picture above). The technician will make sure that as much as possible of

your chest is covered during the scan. We will store these images (using an anonymous identification code) in a secure electronic database for future analysis. You will not be identifiable from these images.

You will be asked to undertake a 10 to 15 minute exercise test on the supine bike (pictured) in which the intensity will progressively go from light to high intensity. You can stop the test at any point if you feel unable to exercise further. Before starting the exercise test, we will make some measurements of your lung function. We will ask you to blow into a special machine called a spirometer (pictured). Before, during and after the exercise test we will measure how much oxygen you are using by asking you to breathe through a special mask. We will also measure your heart rate and blood pressure throughout and take some more pictures of your heart by echocardiography during the exercise. We will also assess the function of the small blood vessels in your muscle using a small device attached to your skin. The device is very safe and works by shining a small amount of near-infrared light into your tissue and measuring how much comes back.

Just as for any exercise, there is a small risk that you will feel unwell (light-headed or faint) following the exercise test, we will monitor you closely to avoid this and you can stop at any time. Very rarely (approximately 1 in 10,000 cases) an exercise test can result in a heart attack or changes in heart rhythm that do not disappear after the test. For this reason, we will not perform this test if there is any evidence you might be at risk. A clinical doctor will be available to respond to any adverse events.

IMAGES OF SOME OF THE TESTS



Optical coherence tomography



Hand grip dynamometer



MRI scan

Magnetic Resonance Imaging (MRI)

MRI uses a powerful magnet and radio waves to form pictures of your body; it is believed to have no harmful effects (there are no x-rays). The scans are highly specialised and they are performed by doctors or radiographers. Before this scan, we will ask you a series of questions to see if there might be any metal in your body (e.g. from previous operations or accidents). The MRI scanner produces a magnetic field which is harmless to the body, but can cause some metal objects to move, including some types of metal that may be found in the body. As long as you have no metal in your body that might cause harm, you can safely have an MRI scan. It is important not to bring metal or jewellery into the scanner room (such as wiring or clasps in your bra, or zips, or buckles in other clothes).

You will be asked to lie down on a flat scanning bed that slides into the tunnel for up to an hour. The scanner can make loud noises. You will be asked to wear headphones during the scan that protect your ears from these noises and allow the person operating the scanner to talk to you. If you have a fear of enclosed spaces (claustrophobia) please let the study team know beforehand. During the scan you will receive an injection of a contrast agent to help visualise your heart. With your permission, we will store MRI images (using an anonymous identification code) in a secure electronic database for future analyses. You will not be identifiable from these images.

Activity monitoring and health app

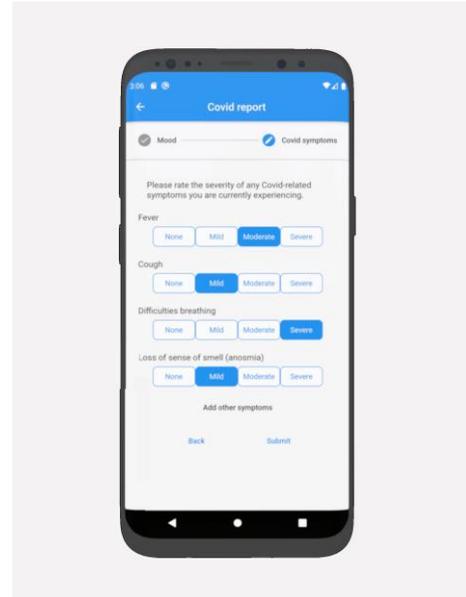
At the end of the visit, unless you have asked to have the monitor posted to you, we will give you a wrist-worn monitor to wear at home (pictured below). We will also ask you to install a special app on your mobile phone. The monitor is very similar in size and appearance to a watch and gives us information about your daily physical activity, heart rate and sleep quality.

The wrist monitor will be used to follow these aspects of your health for around 18 months. The device is waterproof so it does not need to be removed at any time, and it should not interrupt your daily living. If for any reason you need to remove the sensor, please replace it when you can.

The phone app allows you to tell us about your health and functioning on a regular basis using some simple questionnaires. We will ask you to complete these questions every week or 2-weeks for the first month, and then less frequently. We will also use the app to ask you to perform some simple health tests (a 6-minute walk test, a sit-stand test and a stair stepping exercise) at regular intervals (every 2 to 4 weeks for the first month depending on the test and then less frequently).



The wrist-worn monitor



The phone app

What are the possible benefits of taking part?

We will provide you with the results of any clinically relevant tests.

We will not routinely provide you or your doctor with the results of the brain or heart scans as they are for research purposes only. We will let you and your doctor know if we find any abnormalities on the MRI scan that require medical attention.

By taking part in this study, you will be helping to advance research into long COVID.

Please be aware that the investigations we perform are for research purposes only and are not designed to detect abnormalities. They are not a substitute for a test that your doctor might request.

What happens if there is an abnormal finding?

There is a possibility that while looking at your scans or other results we may see a finding that we did not expect. This is called an “incidental finding” and may occur in around 1 in 10 people. Most incidental findings are no cause for concern, but, if we notice a potentially serious abnormality, we will write to you and your GP, usually within weeks of your visit.

We will not contact you about unusual findings that have no definite implications for your health. For example, we would tell you and your GP if we saw an abnormality on one of your scans that looked as though it could be a malignant tumour or another similarly serious condition. On the other hand, we would not tell you if we saw typical appearances of gallstones, a simple cyst or scarring (e.g. on the lung) as these abnormalities are common in healthy people and not considered serious. We would also not tell you about something that is clearly related to a health condition that you have already told us about. Finally, we would not tell you about a potentially serious abnormality if it was identified at a later date by researchers analysing the scans and was deemed non-remedial.

Based on other studies, about two or three out of every hundred people (2-3%) will have an abnormality that is potentially serious and which we would write to you and your GP about. About one in three of these people will turn out to have something serious that they may not have been aware of before, while two out of every three of these people will turn out to have something non-serious. This happens because something that looks suspicious on one of our research scans can turn out to be something like a benign cyst, an artefact of the scanning process (a technical glitch), or something that you or your GP already know about (but we don't).

It is important to understand that we will not notice all potentially serious abnormalities. For this reason, if you do not receive any feedback from us about a potentially serious abnormality, you should not regard this as reassurance about your health. It should not stop you from seeing your doctor about any health concerns that you might have.

Your GP may refer you to specialists for further investigation and treatment. Some abnormalities found on scans might never have been noticed (especially if they never caused you any problems). Other abnormalities might have come to light weeks, months or even years later.

Finding abnormalities on scans can lead to an earlier diagnosis, but sometimes can lead to unnecessary anxiety, investigations and treatments. Some diagnoses could affect your ability to drive, work or get travel, health or life insurance.

You can only take part in this study if you agree that we can tell both you and your GP if we notice a potentially serious abnormality. If you feel that the anxiety of being told about an abnormality, or the disruption to your life caused by further investigations, is likely to outweigh any benefit to you, it would be better not to take part in the study.

What are the risks and are the tests uncomfortable?

All our tests are undertaken by healthcare professionals with the aim of ensuring your safety and comfort throughout your visit. All the measurements are well established and have been performed in many studies.

The blood sampling is a routine and very safe procedure, but may cause bleeding, bruising or pain. Some people may become dizzy or feel faint. Very rarely, infection can occur but to minimise this risk, experienced medical personnel will perform the blood sampling using aseptic technique and, if a sample is not obtained with 3 attempts, no further venepuncture will be performed.

MRI scans are very safe. The MRI scanner is noisy but not at all painful. Some people experience feelings of claustrophobia during the scan, but there is constant contact via an intercom system so you can request the investigation be stopped at any time.

The other tests are considered not to carry significant risks of adverse effects.

There is a potential for causing some distress through the finding of an incidental health problem as a result of the research tests.

What if something goes wrong?

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated by members of staff you may have experienced due to your participation in the research, UCL complaints mechanisms are available to you. Please ask your research doctor if you would like more information on this. In the unlikely event that you are harmed by taking part in this study, compensation may be available.

If you suspect that the harm is the result of the Sponsor's (University College London) negligence, then you may be able to claim compensation. After discussing with your research doctor, please make the claim in writing to Professor Nish Chaturvedi, who is the Chief Investigator for the research and is based at 1-19 Torrington Place (contact details at the end of this document). The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

What will happen if you don't want to carry on with the study?

You can decide to end your involvement in this study at any time. If you decide to withdraw from this study, you will no longer be asked to attend research clinics and we will not contact you in the future for follow-up or for any other reason. We will securely remove any personal information held about you from our database. If you wish to withdraw, your samples will be destroyed. Information about you that has already been collected as part of your involvement may be retained, but there will not be any further processing of your data.

What will happen to the results of the study?

This study will be written up for presentation at scientific conferences and for publication in peer-reviewed health or scientific journals. You will not be identifiable from any published results.

Biological sample storage notice

The anonymised blood and urine samples will be collected, stored, used and disposed of in accordance with the Human Tissue Act 2004. This legislation regulates the rules that determine how your samples are collected and stored. Your samples will be stored in laboratories approved by UCL or HTA licensed establishments. We will seek your consent to take, store and analyse the samples, and the samples will only be used in future in the ways we have outlined above.

Data Protection Privacy Notice

The study is compliant with the requirements of General Data Protection Regulation (2016/679) and the Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing and disclosure of personal information, and will uphold the Act's core principles.

University College London (UCL) is the sponsor for this study based in the United Kingdom. UCL is the data controller; the UCL Data Protection Officer is data-protection@ucl.ac.uk. The data processor will be Abacus Data Entry and Mailing Ltd.

This means that we are responsible for looking after your information and using it properly. UCL will keep identifiable information about you for 6-12 months after the study has finished.

An identification number will be used during the data collection. The data collected during the course of the research project will be kept strictly confidential.

The results of the study will be presented at conferences and published in scientific journals. No information which could identify you will be used in any report that is presented or published.

All the information we collect will be kept confidential and there are strict laws which safeguard your privacy at every stage.

How will we use information about you?

We will need to use information from you for this research project.

This information will include your NHS number, ethnicity, name and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name, contact details or NHS number. 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.

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 information about you that we already have.
- 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 hold about you.
- 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. Data will be stored at UCL and the use of the information and biological samples are managed and reviewed by the CONVALESCENCE data sharing committee, which consists of senior scientists from CONVALESCENCE executive group. The organisations who may share data with may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

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/ or www.ucl.ac.uk/legal-services/privacy
- our leaflet available from <https://www.ucl.ac.uk/legal-services/privacy/ucl-general-privacy-notice-participants-and-researchers-health-and-care-research-studies>
- by asking one of the research team
- by sending an email to I.howes@ucl.ac.uk or the Sponsor Data Protection Officer (data-protection@ucl.ac.uk).
- by ringing us on 020 7679 9288.

Data Sharing

The use of the information and biological samples are managed and reviewed by the CONVALESCENCE data sharing committee, which consists of senior scientists from CONVALESCENCE executive group. UCL will share pseudonymised research data collected about you with Twins cohort. Anonymised data, images and samples may be shared with other bona fide researchers from UCL, other academic institutions, charities and organisations as defined by the MRC, who submit a data request form. The CONVALESCENCE data sharing policies and processes meet the requirements and expectations of MRC policy on sharing of data from population and patient cohorts and ensure that the use of data is within the bounds of consent given by study participants, complies with MRC guidance on ethics and research governance, and meets rigorous MRC and UCL data security standards. Details on who we share data with, how we share, and what is shared, can be found via our website: <https://www.ucl.ac.uk/cardiovascular/research/population-science-and-experimental-medicine/mrc-unit-lifelong-health-and-ageing-ucl/data>.

Who is organising and funding the research?

The research is organised by the study team of the MRC Unit for Lifelong Health and Ageing at UCL. The funding was provided by UK Research and Innovation and the National Institute for Health Research.

Who has reviewed this study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee (REC) which is there to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable ethical opinion by the Oxford A REC and the Health Research Authority (HRA) in accordance with UK research approval and conduct regulations.

How have patients and the public been involved in this study?

Individuals with long-COVID known to the applicants and from local clinics were approached to inform development of the proposal. They rephrased study questions to reflect the patient perspective, advised that we include a clear link between research and policy and asked that we recognise the importance, and controversy, around terminology, including 'long-COVID', 'post COVID-19 syndrome'. Individuals from the cohorts PPI groups have reviewed the participant information sheet and other participant facing materials.

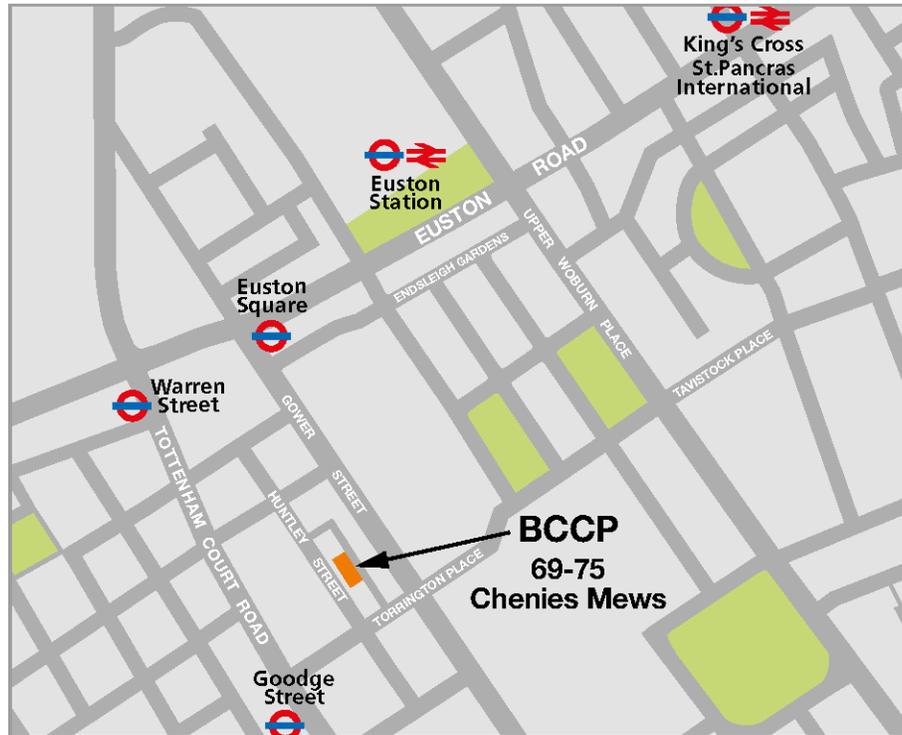
Who can I contact for further information?

If you have any queries about your appointment, please contact:	Name and Contact Details of the Principal Investigator:
<p>Lee Hamill Howes</p> <p>MRC Unit for Lifelong Health and Ageing at UCL</p> <p>Third floor, Bloomsbury Centre for Clinical Phenotyping. The Roger Williams Building 69-75 Chenies Mews London WC1E 6HX</p> <p>Telephone: 0207 679 9288</p> <p>Email: l.howes@ucl.ac.uk</p>	<p>Prof Nish Chaturvedi</p> <p>MRC Unit for Lifelong Health and Ageing at UCL</p> <p>1-19 Torrington Place London WC1E 7HB</p> <p>Telephone: 020 7670 5700</p> <p>E-mail: n.chaturvedi@ucl.ac.uk</p>

Thank you for taking the time to consider participating in this study.

Location of the UCL Bloomsbury Centre for Clinical Phenotyping (BCCP)

The UCL Bloomsbury Centre for Clinical Phenotyping is located at 69–75 Cheries Mews (WC1E 6HX).



The nearest tube stations are Godge Street (Northern line), Euston Square (Northern line), and Euston Station (Circle, Hammersmith & City, and Metropolitan lines).

Buses 14, 24, 29, 73, 134, and 390 serve the Centre.

The nearest mainline train stations are Euston (0.5 miles), King's Cross and St. Pancras International (1.0 mile).