Imperial College London

NHS Imperial College Healthcare NHS Trust

Participant Information Sheet

ACCESS@ICL:
An All-inclusive Cohort for the Comprehensive Examination of Sporadic Small Vessel Disease

CORE COHORT

Principal Investigator: Dr Alastair Webb
Sponsor: Imperial College London

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

We can see the effects of chronic changes to the blood vessels deep inside the brain on a brain scan as people get older. This is called 'small vessel disease' but is present in the majority of older people and is often a feature just of ageing. However, when these changes become more severe they are one of the commonest reasons people have strokes, bleeds in the brain or develop dementia. However, we currently can't treat these changes as we don't fully understand why this happens, or what medications to use. This is partly because these changes vary a lot from one person to another and we don't have good ways of measuring what is wrong with the blood vessels.

This research study aims to improve our understanding of cerebral small vessel disease to identify new ways to treat it. In particular, we aim to include a much broader range of people with small vessel disease than in previous studies, and do more detailed measurements of how their blood vessels work, how the condition affects them, and then to continue to keep in touch with people to understand what medical difficulties they develop in the future.

Why have I been invited to take part?

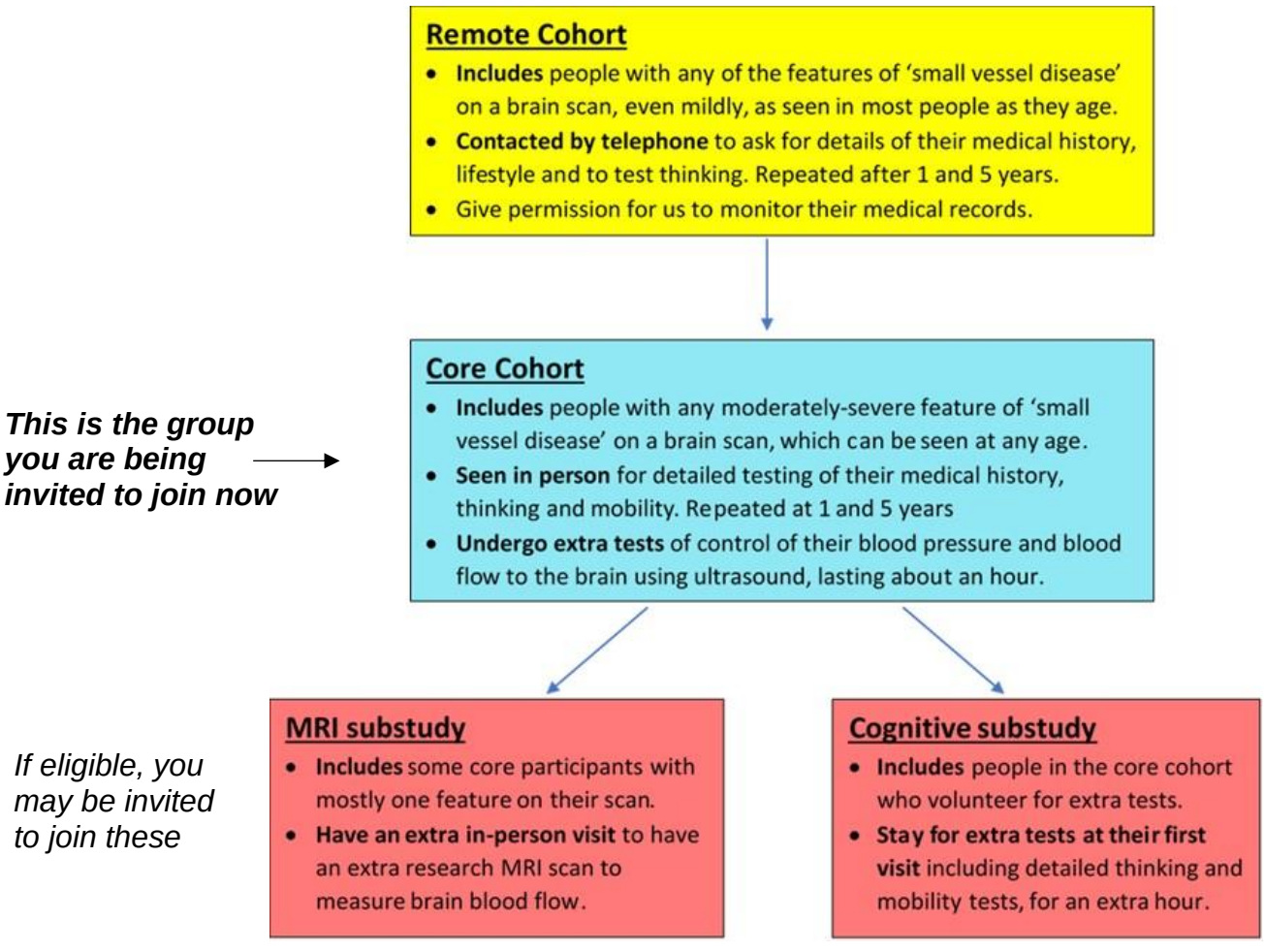
You will have had an MRI brain scan performed when you were previously an inpatient or attended an outpatient appointment at one of our hospitals. This has shown some evidence of cerebral small vessel disease. However, this may be entirely in keeping with your age and is usually **not a cause for concern.** As such, it may not even have been mentioned to you as these changes are very common in most people with age. However, it means you may be suitable to join our research study to better understand how these changes occur and what they mean for people like you

Do I have to take part and can I withdraw?

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

What will happen to me if I take part?

You have been provided this information sheet to give you the information you need to consider whether you would like to take part. The study includes a number of different groups of people, including a 'remote cohort' of people with any degree of changes of small vessel disease on a brain scan, from very mild to severe, and a 'core cohort' of people who have at least moderate changes on a brain scan, although these may still be normal for your age and are not necessarily any cause for concern. People in the 'remote' cohort are contacted only by telephone and by reviewing their medical records, whilst people in the 'core cohort' are seen in person for more detailed tests. Some people in the core cohort may also be invited to have further tests as part of a brain imaging study (the MRI substudy) or further tests of their thinking and mobility (the cognitive/functional substudy). You are being invited to join the core cohort of people seen in person. If you are eligible for the more detailed MRI or cognitive/functional studies, these will be discussed with you at your first visit. If offered the choice to participate in one or both of these additional assessments, you are entirely free to participate or not, and it will not affect either your medical care or your participation in the main study.



If you are interested in taking part in the study, you will be invited to attend an appointment at the Hammersmith Hospital. You will be able to discuss the study with the researchers and, if you haven't already done so, you will be asked to sign a consent form at this time, agreeing to participate in the study. The main assessments for the study will then take place at this visit, which will usually last 2-3 hours in total (the baseline visit).

After the baseline visit, we would like to know what happens to you in the future, including the development of any future medical issues and in terms of your lifestyle and ability to function day to day. Therefore, we would like to see you again 1 year and 5 years later, back at the Hammersmith Hospital for some further assessments. These visits will usually last 1-2 hours. They will consist of the same assessments as are performed at the baseline visit, including a clinical assessments, tests of your thinking and mobility, and the physiological tests described below. If you are unable to attend in person at 1 or 5 years, then we would like to contact you by telephone instead. As it isn't possible to see everyone face-to-face, we would also like your permission to access to your medical records in case you develop problems in the future, and to use your medical data including analysing any brain scans you have performed as part of your medical care. Finally, we would like to contact you by telephone to monitor your future health, even after the 5 years have passed, and to be able to access your medical records and identify if you have had major medical problems or died in the future, until the study finishes.

We have explained below what happens at each visit in more detail.

Baseline Visit

After the study has been explained and you have had a chance to ask any questions, you will be asked to sign a consent form to join the study. You will then have two sets of assessments, each lasting 1 hour to 1.5 hours.

The first set of assessments are clinical tests to determine your medical history and current abilities. This includes a formal review of your previous medical history and medications, as well as questions regarding your lifestyle, such as your diet, smoking, alcohol use, sleep quality etc. We will then ask you to complete a series of tests of your memory and thinking, before a series of tests of your mobility such as some balance tests and some tests of your walking speed. Finally, we will take a set of blood tests. These tests are taken for research purpose, including measures of the chemicals in your blood and extraction of DNA for genetic tests, but you will not get any results from these tests. If something unexpected is identified that is very significant for your future health is identified, we will let you know. However, this is unlikely to be necessary.

The second set of assessments at the baseline visit include a series of tests of how the blood vessels in your brain work. These tests are comfortable, non-invasive tests that most people tolerate without any difficulties. However, if you do not like the testing you can stop at any point. The tests include monitoring of your heart rate with a continuous electrocardiograph (ECG), your blood pressure with a continuous blood pressure monitor on your finger, your exhaled breath with plastic tubing under your nose and the blood flow to your brain with two ultrasound probes attached to a comfortable headband, using the same technology used to examine babies in the womb. These tests measure how much blood flow to the brain pulses, and how much the blood flow to the brain changes with spontaneous changes in your blood pressure.

We will then measure your pulse with a probe placed on the skin over your wrist, the top of your leg and on your neck, which tests how much the blood flow to the body pulses. We will ask you to breathe quickly for 30s and then to breathe 6% carbon dioxide mixed with air through a facemask for 3 minutes, at a slightly higher concentration than you normally breathe out. This tests how responsive the blood vessels in the head are to breathing changes. During the test, you are breathing normal amounts of oxygen and the test is very safe. However, some people feel that they need to breathe more heavily whilst doing the test or notice some tingling in their hands or feet and need to stop.

Additional Cognitive/Functional Study

Anyone in the 'core cohort' is eligible for this additional study, but we need a range of people with different degrees of thinking or mobility problems, so you may or may not be invited to join this study depending on how many people like you have already joined. If you do join this study, it will include approximately 60 minutes of more detailed testing of your thinking and ability to walk and perform daily tasks. These assessments are principally designed to compare the usefulness of the different tests. If asked to participate, then it is your choice whether to do so or not.

Additional MRI study

Some participants in the 'core cohort' may be invited to join this additional MRI study. It will include people who have at least moderately severe changes of small vessel disease on a brain scan, but where there are one of the changes we see on the scan are moderately severe, and otherwise the scan is normal or only mildly affected. If you are eligible for the MRI scan study, you will then be offered the choice to have an MRI scan of your brain at an additional visit to the hospital. The scan lasts approximately 60 minutes, with the whole visit lasting approximately 90-120 minutes. This will be discussed before you sign the consent form at the first meeting with the study team, and we will ask you to specifically consent to this part of the study or not. This specialised scan will test the pulsations of blood flow to the brain and the responsiveness of the small vessels in more detail. However, there is no obligation to participate and you may still complete the rest of the study without having the brain scans. The MRI scans will be performed at the Rob Steiner Imaging Centre, also based on the Hammersmith Hospital site.

What happens during the visit?

The MRI scan is made up of several parts:

1) Scans looking at the structure of the brain

These scans are similar to normal MRI scans. If you have had an MRI scan as part of your stroke or memory care, this scan will be the same, with additional images measuring the blood flow to the brain.

2) Cerebrovascular reactivity brain scan

This scan tests how well the brain blood vessels can open up and increase blood supply to the brain when needed. During the MRI brain scan you will wear an oxygen mask over your nose and mouth. We will give you air to breathe that has a low amount of carbon dioxide, a gas that occurs naturally in the air, added to it. This will make the blood flow to the brain increase, which we can measure on the scans. The technique has been used in many hospitals around the world. There is a doctor present during the brain scans and they will be monitoring your breathing and pulse whilst you breathe the gas. This lasts around 15 minutes.

3) Cerebrovascular function scan

We will perform a scan to assess the blood flow to the brain in more detail. During this scan, you will wear standard blood pressure cuffs. During approximately 7 minutes of the scan, these will partially inflate on one arm at a time, for up to 5 minutes each, whilst standard blood pressure readings are taken in the other arm. In addition, we will monitor your oxygen levels and the carbon dioxide level of your exhaled breath. Finally, you may

be asked to stare at a cross or images on a screen, or to tap a button during a simple task. During this period, a circle of black and white squares will intermittently flash in your range of vision for a few seconds at a time.

4) Blood-brain barrier scan

In small vessel disease, the blood vessels in the brain can become slightly 'leaky' and their ability to prevent molecules entering the brain from the blood can be less effective. We test this by giving an injection of the normal 'contrast' agent that is routinely used in clinical brain scans to test this problem. The scan then measures whether there is any leakiness of the blood vessels. This is usually very subtle in small vessel disease, and if present is not known to be a significant cause for concern. During the scan, you may feel some tingling or the sensation of needing to urinate whilst the contrast is injected, which is normal. In the majority of people the contrast injection is completely safe, but rarely people can have an allergic reaction to the contrast, and it can not be used if your kidneys do not work normally. This will be checked before the scan.

Will I be paid for participating?

Although we are not able to pay you for participating in the study, we will reimburse reasonable travel costs for attending the hospital for any visits that occur in addition to your normal medical care. The researcher involved in the study also receive no additional payment for carrying out the research, beyond their normal salary.

What are the possible disadvantages and risks of taking part?

The physiological tests involved in the study are not associated with any significant risk, and are principally monitoring tests. Whilst breathing carbon dioxide, you may feel breathless, have tingling in the hands or feet, or very rarely develop a headache afterwards, but the test is tolerable in the majority of people, and is not associated with any significant risk. There are no risks associated with the ultrasound scans.

MRI scans and ultrasound scans are safe for the majority of people. They use either sound waves or a magnet and radio waves to generate the brain scan pictures. They do not involve any radiation, meaning there is no risk in having many scans.

Most patients find the oxygen mask and air with carbon dioxide easy to tolerate, either during the MRI scan or during the physiological tests. Some people feel that their breathing is a little harder, like during exercise. A few people feel that the mask is uncomfortable and makes the MRI scan feel more claustrophobic. To minimise this, we keep the mask on for as little time as possible (15 minutes in the MRI scanner, less than 10 minutes during the ultrasound monitoring) and you are given a button to press if you want the scan to stop at any time. There is also a doctor present who monitors your breathing, pulse, and oxygen levels.

If you have the MRI scans, it is important to know that MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part. For example, if you suffer from claustrophobia, you could not be scanned. Normally, MRI scanning for research purposes would not be performed without further investigation if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an

aneurysm clip, hip replacement, or if you carry other pieces of metal that have accidentally entered your body.

While there is no evidence to suggest that MRI is harmful to unborn babies, as a precaution, the Department of Health advises against scanning pregnant women unless there is a clinical benefit. If you think you may be pregnant you should not take part in this study. As some of the scans are noisy, we would give you earplugs, head padding or headphones to make this quieter for you. It is important that these are fitted correctly as they are designed to protect your ears. In preparation for your scan and for your comfort and safety we may ask you to change into pocketless and metal free "pyjama-style" top and trousers, which are available in a range of sizes. You may keep your underwear and socks on, but we would ask ladies to remove underwired bras. If you have a suitable sports type bra you may wear this instead. Metal jewellery, including body piercing, must also be removed. Eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field. If you wish to wear eye makeup to your scan we can provide makeup removal wipes but you are advised to bring your own makeup to reapply. Lockers are provided to secure your personal belongings and clothing.

If you have had a brain scan already, e.g. to diagnose a stroke, then we are very unlikely to find anything different. It is important to note that we do not carry out scans for diagnostic purposes, and therefore these scans are not a substitute for a doctor's appointment. Although our scans are looked at by a study doctor they are not reviewed by a doctor who specialises in the interpretation of brain scans and are intended for research purposes only. Occasionally a researcher may detect a possible abnormality. In this case, we would have the scan checked by a specialist doctor. If the doctor felt that the abnormality was medically important, you would be contacted directly and recommended to have a hospital (NHS) diagnostic scan arranged. All information about you is kept strictly confidential.

If we find something on a scan or during any of your assessments performed as part of the study, then we will either notify your GP, the doctor who looks after your stroke or memory care, or arrange appropriate follow up ourselves. As you will have had a routine MRI scan for the diagnosis of your small vessel disease, it is unlikely that any brain scan will identify anything else.

What are the possible benefits of taking part?

The study is designed to understand how any symptoms you may have had are related to changes on your brain scan, the tests we perform and your future health. As such, it is not specifically designed to improve your medical care. However, we measure many things that are important to reduce the risk of stroke and dementia, such as your blood pressure level, and will monitor these over 5 years. Therefore, if we identify that these things are not fully controlled then we will write to your GP with this information, and where necessary with recommendations for treatment. This may therefore help to reduce your risk of future problems.

To keep you informed, we will provide a newsletter by email about the progress of the research on an annual basis.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the condition that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw your research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

What happens when the research study stops?

A key aim of the study is to understand the long-term effect of the changes we measure at the baseline visit. Therefore, we will ask your permission to be able to access your medical records even after 5 years has passed, and to identify if you have had major medical problems or even died whilst the study continues and for up to 2 years after the last visit of the last patient. If the permissions to run the study continue to be granted, this may therefore continue for multiple decades. However, you can withdraw your consent at any time. If the study is stopped, then the data collected as part of the study will be retained for 20 years, except that any information that can be used to identify you will be removed. Similarly, any blood samples that have been collected will be either destroyed or kept, without any information that may identify you, in a regulated storage facility called a 'tissue bank' that is tightly governed and regulated by the government. Blood samples may therefore be analysed either by the study team, or used by other research teams for future collaborative research studies. In this case, your blood tests will be provided anonymously without any personal identifiable information.

What if something goes wrong?

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 (Dr Alastair Webb, Clinical Reader in Stroke Medicine, Imperial College London). The normal National Health Service mechanisms are also available to you, and you may contact the Imperial College Healthcare NHS Trust Patient Advice and Liaison Service (PALS) at 020 3312 7777. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

What happens to my data?

Imperial College London is the sponsor for this study and will act as the Data Controller for this study. This means that we are responsible for looking after your information and using it appropriately. Imperial College London will keep your personal data for

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

The study is expected to finish in September 2034. For more information regarding the end date please contact the study team, see 'WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED' for contact information.

We will need to use information from you and your medical records for this research project. This information will include your name, NHS number, date of birth and contact details. People within the College and 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.

If the research team become aware that you have lost the ability to consent to the study whilst it is ongoing, most often due to the development of another medical condition that affects your thinking, we will ask a ‘personal consultee’ (someone who knows you well on a personal level and can advise on your likely wishes) to advise us whether they think you would wish to remain part of the study, and sign a consultation form to that extent. This would include continuing to keep and analyse your data and blood samples that we have already collected, and continuing to have access to your medical records and perform searches of centralised NHS and governmental records (for example death certification) to know if you develop further medical problems. Follow-up, face-to-face assessments would be performed only when your personal consultee is certain you would wish to continue to participate, and would be limited to interviews and tests of your thinking and mobility. In circumstances where no suitable person is available who can act as your ‘personal consultee,’ a ‘nominated consultee’ will be nominated in accordance with legal guidance who can advise on your likely wishes and is fully independent of the research project.

Blood samples may be analysed either by the study team, or used by other research teams for future collaborative research studies. In this case, your blood tests will be provided without any personal identifiable information.

Will my GP be informed?

With your consent we will tell your GP that you are taking part in this study when it is necessary. Should the need arise, we will tell your GP (or other relevant healthcare professional) of any clinically significant findings.

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.

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.

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.

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, 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 central NHS records, your hospital or your GP. If you do not want this to happen, tell us and we will stop. This will not affect any healthcare or support you may be receiving separately.

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 this could affect the wider study or the accuracy of data. 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.

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 research team
- by sending an email to accessICL@imperial.ac.uk

Complaints

If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to accessICL@imperial.ac.uk, or else you may contact the Imperial College Healthcare NHS Trust Patient Advice and Liaison Service (PALS) at 020 3312 7777.

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.

What will happen to the results of the research study?

The study is expected to result in research findings over many years, with some of the most important results only becoming available after we know what problems people run into in the long-term. We expect that the results of the study will therefore be disseminated by conference presentations, research publications in scientific journals, reports to regulators and funding bodies, through newsletters to participants and may be disseminated by press release or interview to mainstream media.

Who is funding the research?

ACCESS@ICL is funded by the combined support of a number of funders, including the Department of Brain Sciences, the St.Mary's Development Fund and philanthropic donations, and will require future funding from a range of funders.

Who has reviewed the study?

This study was given a favourable ethical opinion for conduct in the NHS by Essex REC.

Contact for Further Information

If you wish to have further information about the study, please contact the study email address (accessICL@imperial.ac.uk) or else call us on _____.