Stroke-IMPaCT Study

The Study Invitation

This **study** is looking at **links** between the **immune system** and **cognitive decline** after stroke. The results of this study could lead to targeted treatments and improved recovery for people who have a stroke in the future.

- The **immune system** helps to keep the body healthy and fights off infections. It is a collection of special cells, organs, and processes.
- **Cognitive decline** is memory, thinking and processing problems which develop over time.

You have not had a stroke, so we would like you to act as a control participant.

This information sheet will **help you decide** if you want to be part of this study. Please **ask** us as many questions as you like. You can also ask others, such as your friends or family.

Eiligibility

You must not have:

1. **metal implant**s including pacemaker
2. problems with your **kidney** function
3. a known **allergy/ reaction** to the contrast dye (Gadolinium) used during the scan

If you suffer from **claustrophobia,** you may find the scan uncomfortable.

About the research

What is the study about?

- Up to a third of people experience **cognitive decline** after a stroke.
- People don't know why some people experience cognitive decline and others don't.
- Patients **report** that cognitive decline impacts their quality of life.
- There are currently no treatments.

What is the study looking at?

- We have previously made scientific discoveries that suggest cognitive decline may be caused by changes in the immune system which occur early after a person has a stroke.
- These discoveries suggest that it **may be** possible to treat the causes of post-stroke cognitive decline.
- The **aim** of this study is to improve our understanding of the links between immunity, cognition and changes within the brain caused by a stroke.
- This could help lead to targeted treatments for post-stroke cognitive decline.
- To help **answer this question** stroke survivors and people like yourself who have not had a stroke are **giving blood samples**, **having Magnetic Resonance Imaging (MRI)** scans and **taking cognitive assessments**.
- This will let the scientists see whether there is **any relationship** between **cognitive decline** and any c**hanges on MRI scans** and in a person's blood over time.

What will I be asked to do?

Attend a series of visits with our research team at Salford Royal Hospital (see page 4- "Participating in the Study").

These visits will take place over the course of **2 years**.

In general, at these visitsyou will be asked to:

1. Answer some questions about your general health
2. Donate up to 57.5ml (12teaspoons) of blood (see page 6, “Research Blood Sampling”).
3. Have a Magnetic Resonance Imaging (MRI) Scan (see page 8 “MRI Scanning”)
4. Take a couple of physical (e.g. gait) assessments and some cognitive assessments (brain game-style tests)

For more information about what each visit involves, see the “Participating in the Study” section on page 4 below.

Why me?

- You are aged over 45 years old, live in the Greater Manchester area and have not had a stroke. **We would like you to act as a ‘non-stroke control.**
- ”Non-stroke” controls are essential for research. Your participation would help our researchers to work out whether differences they see in the stroke survivor population are due to a person having a stroke or due to natural variation between people.
- If you have **existing health conditions or recent infection**, please discuss this with one of our research practitioners and they will advise you on whether or not you are eligible to take part.

Who will conduct the research?

A **specialist team** of clinicians (e.g., Doctors and Nurses) and researchers who investigate stroke and immunology. The team is led by Professor Craig Smith, of Salford Royal Hospital. The collaborators in this study are based at The University of Manchester, The University of Stanford in California, USA, and Columbia University in New York, USA.

The University of Manchester is the Study Sponsor for all research taking place in the UK.

Participating in the study

If you are interested,

1. the researcher will conduct a short telephone assessment lasting no longer than 15 minutes to check you are eligible to take part.
2. The researcher will ask about current health conditions and medications and check you have not had any recent infections.
3. MR brain imaging involves injection of a contrast agent (Gadolinium).

This can only be given to people with normal kidney function.

   a. The researcher will ask if you have had your kidney function checked in the preceding three months. If it has, we can obtain this result, with your consent at your first visit (1a- see below). If you are unsure or you have not had this checked, this will be checked at your first visit (1a- see below).

4. You will then be invited to attend Salford Royal Hospital at a time convenient to you for the visits below.
5. If you agree, you may be sent some questionnaires in the post. You can complete these before you come to your appointment, or you can choose to complete them while you are with our team.

At the start of your participation: Visits 1a, 1b and 1c.

Some of these visits can take place on the same day. Regardless, they will all take place within about a month of each other (to suit your availability).

Visit 1a- Eligibility & Consent- Approximately 45 minutes

1. The researcher will ask you to sign a consent form giving consent to study participation and an MRI scan safety questionnaire to confirm you are eligible to undergo an MRI scan.

2. We will record information e.g., your age, sex, NHS number, current medications, and other health issues.
3. If you have had a blood tests taken by your GP or hospital in the last 3 months, the researcher will access this result (either from your electronic patient record or by contacting your GP).
4. If you have not had a blood test to measure your kidney function, the researcher will obtain a blood sample (5ml; 1 teaspoon). This sample will be sent to the local clinical laboratory.
    a. You will only be eligible to participate in the study as a Group 3 control if your kidney function is within normal range*. This is because good kidney function is a requirement for the specialised MRI (brain scan) people in this study have (see page 11).
    b. If any abnormal result is found on the blood sample taken at this visit, the researcher will inform you by telephone and a copy of the result will be sent to you General Practitioner.
    c. If your kidney function isn't sufficient enough for you to participate in the study as Group 3 control, we will ask if you would like to participate as a Group 2 control, because Group 2 controls do not have MRI scans.

* If we can confirm your kidney function before your appointment, you may be invited to undergo visit 1b and 1c at this same visit (maximum total visit length 5 hours).

Visit 1b- Baseline Assessment- Approximately 2 hours.

This can be combined with Visit 1a (above) and/or Visit 1cb (below).

You will be asked to:

1. Answer a few questions on your medical history, including any current medications you take

2. Donate a research blood sample (see Page 6 "Research Blood Sampling")3 Undertake a cognitive battery and brief physical assessment (e.g. heart rate, gait assessment).

Visit 1c- MRI Scan- Approximately 2 hours.

This can be combined with Visit 1a &/ Visit 1ba (above).

You will be asked to:

1. Have an MRI scan (see page 8 “MRI Scanning”).

Approximately one year after your first visit: Visit 2

They will both happen on the same day, unless you request otherwise.

Visit 2- Approximately 2.5 hours.

These will be a repeat of Visit 1a and 1bb.

Approximately 1 year after Visits 2a and 2b: Visits 3a, 3b and 3c.

Some of these visits can take place on the same day. Regardless, they will all take place within about a month of each other (to suit your availability).

Visits 3a, 3b & 3c- Approximately 5 hours total.

This will be a repeat of Visits 1a, 1b and 1c.

We may invite you to continue to participate in the study after Visit 3 a/b/c and attend follow-up at yearly intervals. You are under no obligation to agree to this and the researcher will give you more information about this after Visit 3 a/b/c.
We will ask you if we can retain your contact details for three years after your last donation. The reason for this is that the study is ongoing and, subject to securing more funding, we hope to continue it for the foreseeable future.

Research blood sampling

- We will check that you are happy to donate a blood sample at each of the above visits.
- The sample will be approximately 57.5 ml (or 12 teaspoons)

The blood sample will be analysed by a different researcher to the one who takes your consent and blood sample.

- During the consenting process we will ask you to confirm that you are happy for blood samples you give to be treated as a **gift.**

- We will:
    - Use the samples you give and the results of your cognitive assessments to help us understand links between the immune system and cognition.
    - Split your blood up into different parts e.g., plasma, serum, and cells.
    - Compare your blood to the blood of people who have had a stroke.
- Most of the sample is used to measure **inflammation** in the blood.
- We will also measure how the cells of the immune system **function** (work).
- Some of the blood sample will be used to measure **genetic function** (DNA analysis). For example, researchers may look at your genes and compare them to others who have had/ not had a stroke. This will hopefully allow them to identify any patterns and or differences.
- Samples for this study will be analysed by researchers at or from Salford Royal Hospital orThe University of Manchester.
- Some samples may be analysed by our collaborators from Stanford University or Columbia University. Some of this analysis may be done outside of the UK.

Where will my blood be stored?

- Your donated bodily fluids will be stored in our approved laboratory before analysis. This is called a **'biobank'**.
- Some of these bodily fluids will be used very **soon** after you have donated them, while the rest may be stored for a **longer** period.
- If you give us permission, we will be able to **store** your samples in our biobank for as long as we need to.
- This could let us:

- ✓ Use your blood samples, and the data we collect, during your participation in this study, to help us with **future** ethically approved research such as other, related research once this study has ended.
- ✓ **Share** samples with other research groups who may have different specialist knowledge and equipment. Some of these groups may be **outside of Europe**.

- **All** your data will be fully **anonymised**. No-one analysing the blood samples, bodily fluids or looking at the research data will know that it is information about you.

If you **do not** want us to retain your samples and data in the biobank you may opt out by ticking '**No'** on the consent form.

- If you agree now but change your mind later, you may contact the research team and inform them of your decision.
- The **consent form** will also include optional consent for genetic analysis and sharing of samples for use in future ethically approved research. For more information – see page 7.
- Please note: it will not be possible to remove your sample/data after they have been fully anonymised

MRI Scanning

Before your visit

- Your kidney function and red blood cell count must be checked.
- We will use some of the blood sample taken at Visits 1 or 3 for this purpose and ensure the result is checked by member of the research team before you undergo the MR scan.

Day of the scan

1. Please arrive at the MR scanning department approximately 30 minutes before the scan is due to start.

   If you have chosen to undergo follow-up visit on the same day, the **research practitioner** will take you to the radiology department.

2. The radiographer will complete a safety checklist which they will ask you to sign.
3. You will be asked to remove any metal items such as belts, watch, earrings, hair slides before entering the scanning room.

During the scan

1. The radiographer will be present in an adjacent room at all times. They will be able to both see and hear you, and will monitor you during the scan.
2. You will be asked to **lie** on the scanning table and the radiographer will make you comfortable.
3. A small tube (cannula) will be **inserted** into a vein in your arm and connected to a syringe. This syringe will contain the contrast dye which will be given during the scan.
4. The MR scan is **noisy**, so you will be given a buzzer to alert the attention of the radiographer during the scan.
5. To help reduce the noise, you will be given **ear plugs** and headphones will be placed over your ears.
6. The radiographer will place **foam block**s either side of your head and a metal coil with slide down over your head.
7. The scanning table will **gently slide** into the 'doughnut' shaped part of the scanner (see picture below).

8. The radiographer will **leave** the scanning room before the scan begins but he/she will be able to communicate you via the tannoy system.
9. The scan will begin and images of your brain will be collected for approximately 60minutes.

- Each scanning sequence makes a different sound, like drilling and banging.
- Before the final sequence, the contrast dye will be injected into the cannula in your arm and this may feel a little cold.
- During the scan it is important that you remain as still as possible so the pictures are not blurred.

After the scan

1. The radiographer will come back into the scanning room
2. The scanning table will slide out of the scanner.
3. The radiographer will remove the head coil, cannula, earphones and ear plugs.
4. You will be helped from the scanning table and taken to a quiet space outside to sit with your relative/friend.
5. The radiographer will offer you refreshments and check you are feeling well before you are permitted to leave the scanning unit.

Possible benefits to MR brain scanning

- There are no direct benefits to you from undergoing the MR scan.
- However, you will be helping us to learn more about changes to the brain after stroke and how these may be linked to other changes in blood cells and cognitive function.

Possible disadvantages to MR brain scanning:

- MRI is a very safe scan for the majority of the population. However, for certain people, such as people with pacemakers or metal implants it can be harmful.
- For this reason, you will be asked to complete a questionnaire to ensure MRI is safe for you.
- MRI can be very noisy and you will be given earplugs.
- Insertion of the cannula prior to the scan can be slightly uncomfortable and you may experience slight bruising. As is the case with a regular blood test, there is a very small risk of infection at the point where the tube is inserted.
- A contrast dye (Gadolinium) is used during the scan. There is a very low risk of **reaction** to this agent, is routinely used and major allergic reactions are rare, occurring in one in one thousand (1:1000) cases or fewer.
    - We will confirm your kidney function is within normal range before you attend the appointment will minimise the risk associated with giving the contrast agent.
- If you experience **claustrophobia,** the MR scan may be an unpleasant experience.
- You will be asked to **lie still** for a period of 60 minutes and this can be uncomfortable.
- As with all research, there is a small risk that we may **find something unexpected**. In this case, if anything unusual is identified the images will be passed on to a trained radiologist who will check them.
    - There is a chance of less than one in one hundred (1:100) that your MRI scan may show a significant abnormality of which you are unaware. In

such circumstances, you will be referred to the appropriate specialist. Such early detection has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

Please note

- If you experience any distress, the scanning process will be immediately stopped.
- The scan should not be thought of as a "brain check", it is not the right type of scan to check for problems. If you are experiencing any symptoms that you are worried about please see your GP.

Will I be compensated for taking part?

- We can provide **free** transport for you (and your relative/friend) to attend your visits, or we can reimburse travel/parking costs.
- If you a participate in MRI scanning, we will offer you **£30** for attending each research MRI scan to compensate you for your time.

None of the researchers on our team receive payment above their salary for your involvement.

What happens if I no longer want to participate in MR scanning or the study as a whole?

- You are **free** to withdraw from the study at any time without giving a reason.
- If you wish to withdraw from the MR scanning or the study as a whole at any time, please **let the researcher know** (contact information on page 19).
- Withdrawal from the MR scanning or the study as a whole will not affect your health care.

Can a researcher withdraw me from the study? And why?

Yes, a researcher can withdraw you from the study, for example:

- If you become unwell and are in hospital.
- If you experience claustrophobia
- If your kidney function is outside the normal range
- If it is felt that the assessment will cause **unnecessary distress**, for example due to a significant change in your cognition.

A change in your cognition **does not mean** that you have lost capacity. However, to avoid distress if this situation was to arise, we have included a **clause on the consent form**, seeking your permission to take the final blood sample if capacity is lost.

- If you choose to withdraw from the study, or the lead researcher withdraws you from the study, any ongoing or future medical care will not be affected.
- In the event of withdrawal from the study, we **seek permission** to retain any blood samples and data to the point of withdrawal.
- However, these **can be** destroyed at your request, provided they have not been anonymised (names and identification removed).

What happens if I have a Stroke, receive a diagnosis of dementia or something else happens to my health?

We hope that you will **remain well** whilst you are part of the study and afterwards. However, some people may have a Stroke, a heart attack, or receive another diagnosis whilst they are part of the study.

In either circumstance, most people will still be able to continue to participate in this research.

a. **If you have a Stroke**, you will unable to continue to participate as a 'non-stroke control'. If you happen to be sent to Salford Royal Hospital after your Stroke, you may be offered the opportunity to become part of the 'Stroke' arm of the study. This will depend on a range of factors and will be determined by the team at the time.

b. **If you do not have a Stroke**, you will most likely be able to continue to participate as a 'control'.

Our team will ask you to **prioritise any medical care over your participation in our research**. They will check whether you are still happy to continue to participate in this study, and will provide as much advice and guidance as you require.

Data Protection and Confidentiality

What information will you collect about me?

- We will need to collect information that could **identify** you, such as your name, NHS number, contact details and date of birth. This is called "personal identifiable information".
- Some health information, such as if you have any conditions that are considered to be risk factors for stroke (including taking certain medications e.g. statins or blood pressure lower medication).

Under what legal basis are you collecting this information?

- We are collecting and storing this personal identifiable information in accordance with **UK data protection law**.
- These state that we must have a **legal basis** (specific reason) for collecting your data.
- For this study, the specific reason is that it is "a public interest task" and "a process necessary for research purposes".

What are my rights in relation to the information you will collect about me?

- You have several rights under data protection law. For example, you can request a copy of the information we hold about you.
- If you would like to know more about your different rights or the way we use your personal information to ensure we follow the law, please consult our Privacy Notice for Research (https://documents.manchester.ac.uk/display.aspx?DocID=37095 and attached).

- If you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to **The Information Governance Office, Christie Building, University of Manchester, Oxford Road, M13 9PL**.
- You also have a right to complain to the Information Commissioner's Office, Tel 0303 123 1113

Will my participation in the study be confidential and my personal identifiable information be protected?

- In accordance with data protection law, The University of Manchester is the **Data Controller** for this study.
- This means that we are **responsible** for making sure your personal information, including your MR scans are kept secure, confidential and used only in the way you have been told it will be used.
- The study team at Salford Royal Hospital and University of Manchester will have access to your personal information
- This information will be **anonymised** as soon as possible.
- Your **name** and any other identifying information will be removed and replaced with a random ID number that is unique to you.
- Only the research team at Salford Royal Hospital will have access to the key that links this ID number to your personal information.
- Your **consent form** will be retained for 25 years at Salford Royal Hospital.
- The **data** will be retained in paper format, including the hand completed assessment forms and questionnaires.

With your consent, your anonymised research data:

1. will be entered on to a computer database hosted by **Stanford University (USA)**. This will include including brain imaging, blood sampling and research assessments.
    a. Stanford University is outside the **European Economic Area (EEA)** which has different data and privacy laws.
    b. The research data will not include any **personal data** e.g. your name and address.

2. will remain on the **electronic database** for the duration of the study,
3. will be **archived indefinitely** in an approved research biobank once the study ends.
4. could be used to support additional **future research** in accordance with the UK Policy Framework for Health and Social Care Research.
5. will only be used for the purpose of future research into **stroke**, **inflammation** and **brain injury**, and cannot be used to contact you regarding any other matter.
6. Will not be used to make decisions about future services available to you.
7. May be provided to researchers running other, ethically approved studies at Salford Royal Hospital, The University of Manchester or at other organisations.

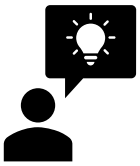
Please note:

- If you do not wish your data to be used in this way, you may **opt-out** at any time.
- It will **not be possible** to remove your data or samples after the link between them and your identity has been broken (fully anonymised).
- Full anonymisation is likely to take place after completion of the final participant assessment and prior to the analysis of samples and data.

Potential disclosure

- If, during the study, we have **concerns** about your safety or the safety of others, we will inform you/ your GP/care team/family member.
- **In all research, there is a small chance that we may find something that we were not expecting. If this is the case, or if we identify anything during your visits that we think requires further follow-up, we may also contact your GP.**
- Individuals from The University of Manchester and regulatory authorities may need to review the study information for **auditing** and **monitoring** purposes e.g. to make sure the project is being carried out as planned, or in the event of an incident. This may involve looking at identifiable data.

Additional Information



- We will **publish/ present** our research findings in scientific & medical journals, as part of PhD theses and at scientific conferences.
    - We will also publish a **summary** of our research on our website https://stroke-impact.org/ but this may not be for some time after the end of the study.
- **Information** that could personally identify you **will not** be included in any publication or report.
- Research staff at Salford Royal Hospital may access your electronic patient record (EPR) up to **3 weeks prior** to your scheduled follow-up visits. This will allow them to check for any recent blood results for kidney function, **send** a letter and **contact** you via telephone to arrange your visit.
- If you **consent** to future contact regarding possible continuation of study participation after visit 3c, the research team at Salford Royal Hospital will access your electronic patient record (EPR)/ use the contact details that you have provided us with and write to you with more information at this point. If you do not consent, the research team will not access your EPR for any other purpose after visit 3c.
- Giving consent at this time will **not obligate** you in any way and you are free to decline.

Will I be told about what the study finds?

Previous study participants have said that they want to **hear** about the study's progress, **learn** about what the researchers discover and **find out** about similar work happening.

- We would like to send you **information** and **updates** about the study such as newsletters, information about what has been discovered, invitations to events where you could meet other participants, and opportunities to give us feedback.
- At most, you will **receive** approximately 6 pieces of information a year (bi-monthly).

- These updates are **separate** from your appointment notifications.
- The consent form asks for your **permission** for us to add your contact details to a secure database so that we can send you these updates.

Please note:

- You are not obliged to **receive** these updates or **respond** to any of the communications.
- You can '**opt out**' at any time.
- Each **communication** will let you know how you can 'opt out' of further communications or change your preferences.
- We will **store** your contact details on this database for a period of 7 years.
    - We ask for permission for 7 years because the Stroke IMPaCT study will end in 2026, and it will take a couple of years for all of the data to be analysed and published.
- You will be **contacted** by phone and/or letter depending on your preferences three times in the 7th year to ask if you would like to continue to receive updates. If you do not respond, we will automatically remove your details from our database.

Who has reviewed the project?

The study has been reviewed by Wales 3 NHS Research Ethics Committee and has received a favourable opinion.

Who is funding the research project?

Leducq Foundation funds the project as part of their Transatlantic Network of Excellence.

What if I have a complaint?

Minor complaints: If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions.

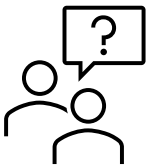
You can contact the research team (details at end of the sheet) during working hours or leave a voicemail if out of hours.

Formal Complaints: If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers then please contact the **Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL**, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 275 2674 or 275 2046.

What do I need to do now?

- Please take time to consider whether you wish to undergo additional research MR brain imaging including discussing with family and friends.
- The research practitioner will answer any questions you may have and to discuss whether you want to take part.

What if there is a problem or you have any questions?



If you have questions about this research then please contact:
The Acute Research Delivery Team practitioners on:

- Telephone: **0161 206 2188 (7 days week)**
- Email: acute.research@nca.nhs.uk

If you are interested in further updates regarding this study and our publications, please visit https://stroke-impact.org/ or follow us on Twitter @ImpactStroke

Thank you for taking the time to read this information sheet