MRC National Survey of Health and Development

Neuroimaging sub-study
Invitation to participate

Bloomsbury Centre for Clinical Phenotyping London

We are writing to invite you to take part in a round of health information collection in London for a neuroimaging sub-study. This is a clinical sub-study that will complement the regular home visits and postal questionnaires.

The MRC NSHD neuroimaging sub-study began in 2015. To date, two phases of data collection have been completed (phase 1: 2015-2018; phase 2: 2018-2020), and 502 members of the NSHD have participated in the Neuroimaging sub-study. We have received some additional funding that allows us to undertake another round of data collection in London.

Details are provided below, but in brief, the first day of assessments will include some memory tests, clinical examination, exercise assessments and a brain scan. The second day of assessments, all of which are optional, will finish in the early afternoon. You will be offered the opportunity to participate in as many or as few tests as you would like, including some additional memory tests, assessments of blood flow, cardiovascular tests, a bone density scan and a lumbar puncture.

Before you decide if you would like to participate, it is important for you to understand why the research is being done and what it will involve. Please take whatever time you need to discuss the study with your family and friends. Your participation is voluntary.

For this clinical sub-study, the research team responsible for the MRC National Survey of Health and Development (NSHD) is collaborating with neurologists who work at the National Hospital of Neurology and Neurosurgery, and Institute of Neurology at University College London (UCL).

UCL
UCL Bloomsbury Centre for Clinical Phenotyping

Contents

What is the MRC NSHD Neuroimaging sub-study?

For most people, health changes gradually with age, often in subtle ways that we scarcely notice. We have already studied those changes by comparing the measures of health taken throughout your early life, and in adulthood, most recently at the 68–69 years home visit. From that we learned a lot about the processes of ageing, building on our knowledge of how factors across life influence health and function. Now we would like to measure health again, with a particular focus on memory and thinking, using a variety of measures to look at brain structure and function.

The specific aims of the Neuroimaging sub-study are firstly to identify the brain changes that accompany healthy ageing; and secondly to see if we can detect brain changes that in due course might help predict who is at risk of developing dementia, and Alzheimer's disease in particular.

We will then explore the genetic, environmental and lifestyle factors that contribute to this increased risk. We aim to be able to identify preventive measures to maintain good health and activity for as many years of later life as possible, and so to influence national health policy. We hope also to gain valuable biological information about early cognitive (memory and thinking) decline, which may in due course help determine how best to design drugs to prevent Alzheimer's disease and other forms of dementia, and how best to conduct drug trials aiming to see if these therapies are effective.

Why have I been invited to participate?

This is a clinical sub-study of the MRC National Survey of Health and Development (NSHD), the British 1946 birth cohort study. You have been invited to participate because you are a member of this cohort study. For this new round of data collection, we will invite some members of the NSHD who previously attended visits in London for the Neuroimaging sub-study, as well as some members who have not had any previous involvement in the Neuroimaging sub-study.

Do I have to take part?

No, your involvement is voluntary and it is up to you to decide if you would like to participate in this sub-study. You do not have to participate in all assessments that are being offered, and you can opt out of some or all of the assessments at any time. If you decide not to participate, this decision will not in any way affect your ability to continue to participate in the main NSHD data collections or any other NSHD clinical sub-study. It will not affect any NHS treatment you receive if you do not take part.

What will I have to do if I take part?

Participating in the Neuroimaging sub-study will involve you making a trip to London for a series of assessments and a brain scan. We would additionally like to invite you to take part in an optional second day of assessments that will end in the early afternoon.

In some situations, we may make arrangements to seek your consent to carry out some of the assessments that do not require specialised equipment or in-person contact remotely. The remote assessments

may be administered through telephone calls, computer-based video calls, or both. If you are interested and willing to participate in some assessments remotely, we will work with you to find the mechanism that would be most convenient for you in your personal circumstances.

We will find dates that suit you, reimburse you for travel expenses, provide meals and refreshments, and will arrange for up to three nights' stay in a hotel. We would encourage you to bring a partner or someone who knows you well. The person accompanying you would also have their travel and accommodation expenses reimbursed.

At the visit we would like to:

1) ask you about your health, medications and any concerns you have about memory; perform a neurological examination; and test your walking and muscles in response to exercise;
2) perform some tests of memory and thinking;
3) take blood and urine samples; and
4) perform brain scans in two different scanners, lasting in total no more than 70 minutes.

If you decide to stay for a second day of testing, we would like to:

1) perform ultrasound scans of your heart and the arteries in your neck (repeating the measures that were performed in 2006–2010);
2) perform a retinal scan;
3) ask you to wear a cap to measure blood flow to the brain while you do some tests of thinking and memory;
4) perform a bone density scan (as was done in 2006-2010); and/or
5) perform a lumbar puncture.

You can opt to have some or all of these tests.

In addition to these tests, we would like to ask you to wear a monitor on your wrist, which is the same size as a watch, to measure your sleep over a 7-day period. We would also like to ask you to wear a non-invasive glucose sensor over the same 7-day period.

More detail concerning what is involved with each of these investigations is provided below.

Pre-visit discussion

If you are interested in taking part, we would first give you the opportunity to discuss what is involved with a member of the research team by telephone. He or she will explain what the study involves, answer any questions you have, and will ask you some questions about your health and your medical history to ensure you are eligible to participate (e.g. make sure there is no reason why you cannot have an MRI brain scan). If, following this discussion, you are eligible and willing to take part, we will arrange convenient dates for you to come to London.

We would like to speak with someone who knows you well either a few days before your visit takes place (over the phone) or on the morning of your visit (over the phone or in person). If you previously participated in a Neuroimaging sub-study visit, we would prefer this to be the person who we spoke with during your last visit, but it can be any family member or friend who knows you well.

We would like to ask this person a few questions about your memory, problem solving, hobbies and personal care. We would also like to ask them whether you have any previous history of delirium following a medical illness. This discussion will take approximately 15 minutes.

The visits

On the day of your visit you will be asked to come to the Bloomsbury Centre for Clinical Phenotyping. This is a facility owned by UCL that has been specifically designed for studies of this kind. You will have the opportunity to discuss any questions or concerns you have about participating at that stage. If you decide to continue with the assessments, you will be asked to complete and sign a research consent form. We will give you a copy of the consent form to keep. If you have not already provided this information, you will also be asked to nominate a family member or friend who you would like to act as your consultee in the future, should you lose the ability to provide consent.

A typical overview of Day 1 is as follows:

DAY 1
Please only have a light breakfast without caffeinated drinks before arriving for your visit on day 1

Arrive at Bloomsbury Centre for Clinical Phenotyping
Greeting and tea or coffee

↓

Consent and history
approximately 15 minutes

↓

Tests of memory and thinking
approximately 1.5 hours

↓ Break 20 minutes

Physical examination and walking test
approximately 2 hours
(This will include a blood sample if you are not attending day 2)

LUNCH
approximately 1 hour

Clinical assessments
approximately 1 hour

↓ Break 20 minutes

Brain scan at the BCCP
approximately 20 minutes

↓

Transfer to UCLH Macmillan Cancer Centre
2 minute walk

↓

Brain scanning
total time in the scanner will not exceed 50 minutes

END OF DAY 1

Clinical assessments and physical examination

We will ask you to update details of your family tree including familial history of dementia, Alzheimer's disease and Parkinson's disease and any medications you are taking. We will ask you some questions about your memory and thinking skills. With your permission, we will discuss other relevant research studies, which you may wish to consider or receive further information about. This part of the study will take no more than 1 hour, with suitable breaks.

With your permission, we will measure your height, weight, and blood pressure; we will conduct a lung function (breathing) assessment; and we will perform a standard neurological examination, which we will video. The videos will be used for research purposes only and all original recordings will be destroyed; digitised copies will be stored on a secure server at UCL. We will ask you to take off your shoes and socks and allow us to examine your arms and legs, but you will not need to undress. We would like you to do some walking tests while wearing an accelerometer, which is a small device attached to your waist. We would also like you to do an exercise test during which you would wear two non-invasive devices: a mask to monitor oxygen changes and an inflatable cuff on your upper arm to monitor blood pressure. These assessments will together take no more than 2 hours, with suitable breaks.

Tests of memory and thinking

We will perform a variety of tests of memory and thinking. Some of these will be paper and pen assessments; others will be computer based. These assessments will take about 1.5 hours, with breaks if necessary. With your permission, we would like you to wear a wrist band during these assessments that measures your heart rate and skin conductance.

When we schedule your visit, we would also like to schedule a phone call with you exactly seven days after your visit. During the call, we will ask you to open an envelope that you will be given on the day of the visit. We will then ask you to provide some answers based on the content of the envelope. This call will take no more than 15 minutes of your time.

Donating blood, RNA and urine

With your permission, we will take a non-fasting blood sample (55 ml, equivalent to 4 tablespoons), and collect a sample of urine. Some of the blood may be sent to laboratories for routine blood tests (such as measures of blood count, kidney function and glucose); some of the blood may be sent to laboratories to derive cell lines that will be used to generate different types of cells (for example, nerve or muscle cells); and some of the blood and urine will be stored in the Institute of Neurology and used to try to develop new tests for detecting early dementia. The samples may be shared, in pseudonymised form, with other specialist centres (academic and commercial collaborators) within and outside the UK.

The remainder of the blood will be used to extract RNA, which will be sent for sequencing. This sequenced information will then be safely and securely stored by the study team, and used to try to understand the genetic causes of early dementia.

What are the risks of having a blood test?

Blood taking is a routine and very safe procedure and will be performed by trained personnel. Some people can feel faint during the procedure, which will therefore be performed sitting or lying down. There is a small risk of bruising.

Wearable devices

As described below, we would like to ask you to wear two devices at home: a sleep monitor and a glucose monitor for 7 days following your visit. During that time, we would like you to keep a diary of your activity and sleep times. A freepost envelope will be provided for return of the monitors and sleep/activity diary after you have gone home.

Sleep monitor

We will ask you to wear a small device on your wrist for 24 hours each day for 1 week. This device, which is about the size of a large watch, will monitor your wake and sleep patterns. The device is waterproof so it does not need to be removed at any time, and it should not interrupt your daily living.

Glucose monitor

We will ask you to wear a portable glucose monitor, about the size of a £2 coin, to measure your glucose levels. This is a small patch that you would wear on your upper arm for 24 hours each day for one week. Some people have reported skin reactions (such as redness or itching) to the sensor adhesive. If you experience any unpleasant skin reactions as a result of wearing the monitor, we advise that you remove the device and contact us if you have further questions or concerns.

Brain scanning

If you have previously participated in the study, the brain scan will be similar to the scan you had done previously, although the scanning may be split into two or three shorter sections rather than one longer scan.

What type of scan will I have?

During the visit, we will invite you to have a brain scan on two different scanners. One scan will take place on an MRI scanner on the ground floor of the Bloomsbury Centre for Clinical Phenotyping. MRI stands for Magnetic Resonance Imaging and produces an electronic picture of brain structure created using a strong magnet instead of an X-ray. This scan will only last approximately 20 minutes. The other scan will take place on a special PET/MRI scanner housed at University College London Hospital Macmillan Cancer Centre, which is located around the corner from the Bloomsbury Centre for Clinical Phenotyping. This scanner allows PET and MRI scanning to be done at the same time. PET stands for Positron Emission Tomography.

A PET scan can be used to demonstrate if certain proteins are building up in the brain. The PET/MRI scan will last no more than 50 minutes in total (one continuous scan or it may be two separate scanning sessions with a break period out of the scanner of up to an hour).

Why am I having this scan?

In this study we are using the PET scan to look at the levels of proteins (β amyloid or tau) that occur in the ageing brain and Alzheimer's disease. If you previously participated in visits to London for the Neuroimaging sub-study, you will undergo a scan that uses a very small amount of radioactive substance called [18F]MK-6240 to show up the tau protein. If this is your first clinic visit for the Neuroimaging sub-study, you will undergo a scan that uses a very small amount of radioactive substance called Neuraceq (18F Florbetaben) to show up the β amyloid protein. The MRI scan allows us to assess brain structure, connections and blood flow, and to see if there has been any damage to the blood vessels.

What will happen before, during, and after the scan?

Before you have a scan, the researchers will ask you some questions to make sure it is safe for you to have the MRI. Metal items may interfere with the MRI and some can be potentially hazardous. These include but are not confined to: cardiac pacemaker, aneurysm clip(s), implanted insulin/drug pump, neurostimulator (TENS unit), hearing aid/cochlear implant, surgical clip or staple(s), heart valve prosthesis, dental braces or any type of removable dental items. It is essential that you tell the study team if there is any possibility that you might have metal in your body. You will be asked to remove any dentures,

hair clips, combs, jewellery, and watches just before you enter the scanner. You can eat and drink as normal before a PET/MRI scan.

Before you enter the PET/MRI scanner, a small cannula (tube) will be inserted into one of the veins in your hand or arm. A small dose of the radioactive substance (either MK-6240 or Neuraceq) will be injected through the cannula.

When you are ready to go into the MRI scanner at the Bloomsbury Centre for Clinical Phenotyping and the PET/MRI scanner at University College Hospital, you will be asked to lie flat on your back on the scanner bed, which will then slide into the scanner. Your time in the scanner will be split into two or three scanning sessions with breaks in between, depending on the type of scan you receive, and your total time in the scanner during the study visit will not exceed 70 minutes.

While you are in the scan, you will be able to press a button to tell the study team if you feel uncomfortable or want the scan to stop. You will need to lie as still as possible during the scan as this helps to ensure that the images we collect are of a good quality.

The scanner makes loud knocking noises during the scan; we will provide you with earplugs or ear protectors which will help to reduce the level of noise for you. Before you leave the scanning department, you will be given time to rest and ask any questions you may have about the study. We will give you a telephone number for you to call if you have any problems or concerns and wish to speak to one of the researchers.

What are the risks of the scan?

Venous cannulation is a routine medical procedure that has minimal risk when performed by trained personnel. A cannula is a flexible tube containing a needle that is inserted into a vein in your hand or arm. The radioactive substance will be injected through the cannula. Some people feel lightheaded following insertion of a cannula and there is a risk of fainting. To minimize these effects, the cannula will be inserted in the vein while you are sitting down. Having a cannula inserted can cause some discomfort and there is a very small risk of blood clots, bruising and infection.

If you take part in this study, you will have either an amyloid (Neuraceq) or a tau (MK-6240) PET/MRI scan. These procedures use a small amount of ionising radiation to form images of your brain. The participants in the amyloid group will be exposed to a radiation dose of approximately 5.8 mSv; the participants in the tau group will be exposed to a radiation dose of approximately 5.4 mSv. These exposures are equivalent to 2 years of natural background radiation in the UK. Exposure to radiation can increase the risk of developing cancer but the doses of radiation you will be exposed to are well within recommended safe limits, and the chances of this happening to you as a consequence of taking part in this study over your lifetime is estimated to be about 1 in 5000 (0.02%). The following paragraphs provide specific information about the radioactive substances.

[18F]MK-6240 has been used in PET scans for several thousand people. It has been used for research purposes in over 3000 people, of whom one experienced a headache after the injection, one experienced a night of insomnia, and two experienced a metallic taste/smell during the injection.

Neuraceq (Florbetaben 18F) has been used in PET scans in research and routine clinical settings for many years. It was licensed for clinical use in Europe in March 2014. The use of Neuraceq in several thousand people has been shown to be safe. A common side effect is discomfort at the injection site (approximately 3.4%) and redness (approximately 1.7%).

There have been no known harmful reactions to MK-6240 or Neuraceq. Despite this, there is still the possibility of a rare allergic reaction.

As with all studies involving radioactivity, specific permission has been obtained to ensure that the levels of radiation to which you will be exposed are safe, and a nominated expert nuclear medicine doctor at the Institute of Nuclear Medicine will oversee this part of the study.

You may feel claustrophobic or uncomfortable lying in the PET/MRI scanner. You can ask to stop the scan at any time.

Please inform one of the researchers if you have had any research or clinical scans in the last 12 months as this may affect your eligibility to take part in the study.

Additional measures on Day 2 (optional)

We would like to invite you for a second day of additional measurements.

You may choose to have all, some or none of these tests.

A typical overview of day 2 is as follows:

DAY 2
Please only have a light breakfast without caffeinated drinks before arriving for your visit on day 2

Return to Bloomsbury Centre for Clinical Phenotyping
Greeting

↓

Consent
approximately 15 minutes

↓

Lumbar puncture procedure
approximately 45 minutes
(This will include blood and urine collection)

↓ Break 10 minutes

Assessments of cardiovascular health (heart imaging)
approximately 1 hour

LUNCH
60 minutes

Tests of memory and thinking and assessments of functional near-infrared spectroscopy (blood flow testing)
approximately 1.5 hours

↓ Break 10 minutes

Physical capability tests, an eye scan and a DEXA (bone density) scan
approximately 1 hour

↓

END OF DAY 2
(early afternoon)

Assessments on Day 2

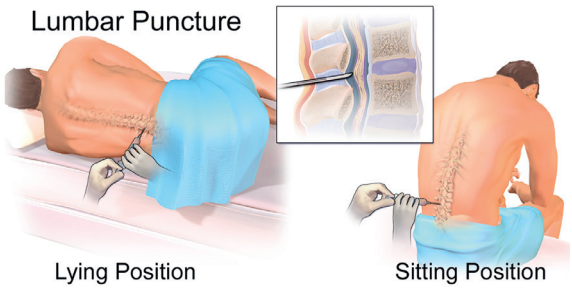
Lumbar puncture

What is a lumbar puncture?

This is a procedure in which a small amount of cerebrospinal fluid is removed by inserting a needle in the lower back. Cerebrospinal fluid is a clear and colourless liquid produced in the brain that circulates around the brain and spinal cord. As it is in direct contact with the brain, it can provide unique and invaluable information about brain chemicals. We will use the fluid to look for biological markers of ageing and very early dementia and we may share this fluid, in pseudonymised form, with other specialist centres (academic and commercial collaborators) within and outside the UK.

What happens during the procedure?

You will be asked to have a light breakfast before you arrive.
For the procedure, you will be asked to change into a gown and to lie on a bed curled up on your side, enabling the clinician to clean your lower back with antiseptic.



Blausen.com staff (2014). *Medical gallery of Blausen Medical 2014*. WikiJournal of Medicine 1(2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436.

Alternatively the trained specialist performing the test may decide that it will be easier for you to have the lumbar puncture in a sitting position leaning forward. The person performing the test will then

inject a local anaesthetic (lignocaine – similar to the injection used for dental procedures) into the skin of your lower back. When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back below the level where the spinal cord ends. 20ml (2 tablespoons) or less of spinal fluid will be removed for analysis and storage. Your body will replace this spinal fluid within 1–2 hours. The procedure, from start to finish, will take no more than one hour. We will ask you to rest for up to one hour. Please refer to **http://tinyurl.com/Insight46LP** to see a video of someone having a research lumbar puncture for a related study.

What happens afterwards?

After the procedure, you will sit or lie flat for about an hour to decrease the risk of headache. You will be given a glass of water to drink after the procedure. You should not do any strenuous physical activity for 24 hours after the procedure. This includes lifting, bending, doing housework, gardening, or doing exercise such as jogging or bicycling. The study team will contact you the day after the lumbar puncture, and subsequently as required, to ensure you are well.

What are the side effects?

The most common side effect of a lumbar puncture is a headache which is worse on standing/sitting but improves significantly on lying down. About 1 in 10 of those receiving a lumbar puncture (for any reason) report a headache. Such headaches are usually mild and last 0-2 days. If you experience a typical post-lumbar puncture headache, you will be advised to take bed rest, and painkillers if needed. In rare cases (less than 1 in 250 of all individuals) the

headache may be persistent for more than 7 days despite simple painkillers and bed rest. In such cases the headache can be treated by a blood patch, which involves a specialist injecting a small amount of your own blood into the spinal canal, under local anaesthetic. On the remote chance that this was required, we would arrange for this to be done either at the National Hospital for Neurology and Neurosurgery in London, or at your nearest appropriate neuroscience centre where it can be performed.

Mild backache following the lumbar puncture may occur. Nerve damage after a lumbar puncture is extremely rare. Sometimes during the procedure the nerves that float in the spinal fluid can touch the sides of the needle causing them to be stimulated and when this happens a feeling like an electric shock or tingling may occur lasting for a few seconds.

The risk of bleeding and bruising following a lumbar puncture is very small. You will not be offered a lumbar puncture if you are taking certain medications, including warfarin or clopidogrel, or if you are known to have a bleeding disorder or a clotting problem. The risk of infection being introduced by the lumbar puncture needle is extremely rare. Other extremely rare complications (reported by fewer than 10 individuals in the world) are mild double vision or mild hearing loss, which come back to normal after few days. All precautions are taken to anticipate potential problems and minimise these risks.

We have previously performed many research lumbar punctures on patients and healthy volunteers in several other studies.
You can ask to stop the lumbar puncture at any time.

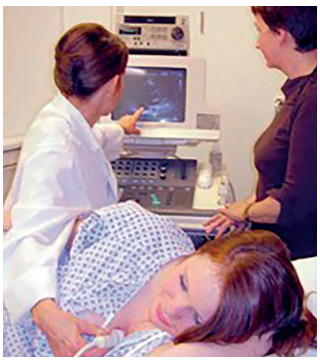
Cardiovascular tests

We will look at your heart function by doing an electrocardiogram (ECG). The ECG is a tracing of the electrical activity produced by the heart while it beats. We will conduct up to two types of ECG. One type will involve placing a few small, sticky sensors called electrodes on your chest, as well as arms and legs. The other ECG method will involve wearing a special jacket so that more detailed ECG information can be collected from across your whole chest. Each test will only last a few minutes.

We will also look at your heart and artery function by using a small hand-held ultrasound scanner across your chest and neck. These assessments will be the same as you had at age 60–64. Ultrasound scans do not use radiation and are safe and painless.

For the ultrasound of your heart, you will be asked to lie on your left side while a probe and a small amount of gel are placed on your chest. The probe will be moved to different positions to allow for moving images to be taken of the heart from different angles. The ultrasound of your heart shows the thickness of the walls of the heart and the size of the heart chambers. It tells us how well your heart is working.

For the ultrasound of your arteries, the probe and a small amount of gel will be placed on your neck and chest. As with the heart ultrasound, the probe will be moved to different positions to be able to see different angles of your arteries. This ultrasound looks at the health of your arteries.



We will also measure the speed of blood flow by applying a cuff around your leg and a small Velcro band (like a necktie) around your neck. This assessment will be the same as you had at age 60–64.

In total, these cardiovascular assessments will take about 60 minutes to perform. If you choose to do the lumbar puncture, we will do the ECG and the ultrasound while you are resting after the lumbar puncture. If you choose not to do the lumbar puncture, these tests will be done on their own on day 2 of your visit.

Additional tests of thinking and memory

During the optional second day of assessments, we will do some additional tests of thinking and memory. Many of these tests were done during previous home visits, and they will take about 20 minutes to perform.

Functional near-infrared spectroscopy (NIRS)

We will perform a test that looks at oxygenation of your brain during a few memory and thinking tests. This will involve you wearing a cap that is embedded with multiple optical fibres that examines changes in the reflection of near-infrared light from your brain. It is completely safe and painless, and it will last for about 30 minutes.

Physical capability tests

We will measure your grip strength, leg power, walking speed, ability to stand up from a chair and standing balance through some simple exercises. These tests will take about 15 minutes to perform.

Eye scan

We will use a retinal ocular coherence tomography (OCT) angiography machine, which is used routinely by many high-street opticians. It takes picture of the back of the eye including the small blood vessels. It does not require dilatation of the pupils or injection of any dye. This test will take about 15 minutes to perform.

DEXA (dual energy X-ray absorptiometry) scan

DEXA scans are used to examine bone and muscle quality and body lean and fat mass. The DEXA scan involves lying on an examination table while the scanner head passes over and around you, without touching you, scanning the whole body, lower spine and hips. The findings show bone size, shape, density and mineral content and can be used to diagnose osteoporosis, weak bones. The scan will take about 30 minutes to perform.

What are the risks of a DEXA scan?

DEXA scans are safe and use a very low amount of radiation, equivalent to less than two days exposure to natural background radiation. The low levels of radiation (lower than a standard chest X-ray), means the radiographer is able to remain in the room during the scan.

Ending involvement in the Neuroimaging sub-study

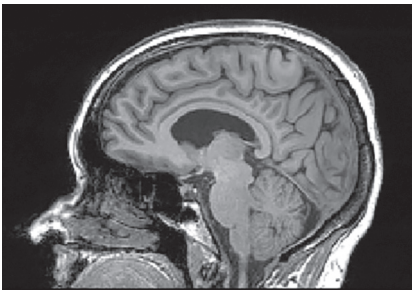
You can decide to end your involvement in this sub-study at any time. A decision to withdraw would not affect any ongoing care, or stop you from continuing with the main NSHD data collections. Information about you that has already been collected as part of your involvement in the Neuroimaging sub-study may be retained. If at any point during your participation, the Chief Investigator or the study sponsor or the director of the study determines that it is not in your best interest to continue the study, or if it is determined that no further valuable data can be obtained, they will stop your participation in the study, with no cost or consequence to you. This would be explained to you at the earliest possible opportunity.

Involvement of your General Practitioner (GP)

If you choose to consent to participate in this reserach visit for the Neuroimaging sub-study, we will ask for your consent to inform your GP of your involvement in the study. If you are not happy for your GP to know that you are participating in this study it will not be possible for you to take part.

What are the possible benefits of taking part?

We will provide you with the results of any clinically relevant tests, and with your consent we will send a copy to your GP. The test results that will be available immediately will be blood pressure, lung function, and height and weight.



Some measures have to be interpreted by a specialist or go to a laboratory for examination, so these results will be provided in the following ways:

- The blood test will need to be interpreted by a specialist. The results from those blood tests which are done in clinical practice will be sent to you and your GP (with your consent). If you are not happy for your GP to know, you can nominate a member of our clinical team to act as your clinical advisor for these results.
- Bone density (DEXA) scan: We will send your bone density scores to you and your GP.
- Retinal eye scan (OCT): The scans will be checked by an ophthalmologist. If there are any abnormalities we shall inform you and your GP.
- Electrocardiogram (ECG), echocardiogram and carotid ultrasound: the scans will be checked by a cardiologist. If there are any abnormalities we shall inform your GP.

- Neurological examination: We will inform your GP if the neurological examination reveals any significant abnormalities that the investigators consider it would be in your interests to know.
- MRI scans: The scans will be checked by a radiologist. We will not routinely provide you or your doctor with the results of the brain scans as they are for research purposes only, but will let you and your doctor know if there are any major abnormalities on the MRI scan (e.g. the presence of a tumour or a large aneurysm) which might affect your clinical care.

You should be aware that being in a research study does not take the place of routine physical examinations or other appointments with your doctor, and should not be relied upon to diagnose or treat medical problems.

New Information

New information acquired during the course of the research that may affect your involvement in the Neuroimaging sub-study will be discussed with you as soon as possible after the findings become available to the study Chief Investigator.

General Data Protection Regulation – Research at UCL and your data

University College London (UCL) is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake 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 properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting:
data-protection@ucl.ac.uk or
Data Protection Officer, UCL Gower Street, London WC1E 6BT.

Further information is provided in UCL's health and care research privacy notice:
www.ucl.ac.uk/legal-services/privacy/participants-health-and-care-research-privacy-notice

The lawful basis that will be used to process your personal data are: '*Public task*' for personal data and' *Research purposes*' for special category data.

The Dementia Research Centre and the MRC Unit for Lifelong Health and Ageing at UCL will collect information from you and/or your medical records for this research study in accordance with our instructions.

The Dementia Research Centre and the MRC Unit for Lifelong Health and Ageing at UCL will keep your name, NHS number and contact details confidential and will not pass this information to UCL. The Dementia Research Centre and the MRC Unit for Lifelong Health and Ageing at UCL will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. UCL will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

The Dementia Research Centre and the MRC Unit for Lifelong Health and Ageing at UCL will keep identifiable information about you from this study for 20 years after the study has finished.

UCL will collect information about you for this research study from the NHS. The NHS will not provide any identifying information about you to UCL. We will use this information to identify factors that affect lifelong health and ageing.

How will your information be shared?

When you agree to take part in a research study, the information about your health and care, your scans, blood tests and genetic results may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities in the UK, Europe, USA and Australia; NHS organisations; secure data platforms (e.g., Dementias Platform UK); charities in the UK and overseas; and companies involved in health and care research in this country or abroad (including, but not limited to, Cerveau, the company manufacturing the tau tracer used in this study).

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 or in accordance with contractual arrangements for commercial purposes. Your information will only be shared in a pseudonymised or anonymised form, so the information shared will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Expenses and Payments

You will not receive any payment for participating in this study. However, travel and hotel costs and the costs of meals/drinks during your visit, for you and the person accompanying you, will be reimbursed. We will discuss your travel arrangements with you and either arrange or help you to arrange travel and hotel bookings for you and the person accompanying you.

What if there is a problem?

If you or your relatives have any concerns about the Neuroimaging sub-study you can speak to a member of the research team who will do their best to answer any questions. Contact details are at the end of this information sheet.

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 during your participation in the research, the National Health Service and UCL complaints mechanisms are available to you. Please ask a member of the research team if you would like more information on this.

In the very unlikely event that you are harmed by taking part in this study, compensation may be available to you. If you suspect that the harm is the result of the Sponsor's (UCL) or the hospital's negligence then you may be able to claim compensation. After discussing with the research team, please make the claim in writing to Professor Jonathan Schott who is the Chief Investigator for the Neuroimaging sub-study and is based at the Institute of Neurology. 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. NHS Indemnity does not offer no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm.

What will happen to the results of the study?

We shall, as in the past, continue to publish the results of our research in medical and research journals, and let you know each year (with the birthday card) what we have published and where. References to all the publications will continue to be available on our web site (**www.nshd.mrc.ac.uk**). No one in the study will be identifiable in any report or publication.

Who is organising and funding the research?

The Neuroimaging sub-study is being organised by researchers at the MRC National Survey for Health and Development, the Institute of Neurology and the Institute of Nuclear Medicine, UCL. It is sponsored by UCL. Funding for the study is from the Alzheimer's Association. Additional funding for some of the assessments may come from the Medical Research Council and the British Heart Foundation.

Who has reviewed the study?

This research project has been reviewed by the London Queen Square Research Ethics Committee.

What happens next?

If you are interested in taking part, a member of the research team would like to talk to you on the phone and answer any questions you may have about the study and to discuss any medical conditions that may affect your participation. Following this discussion, and if you agree to participate, a member of staff from the research unit will contact you to arrange a mutually convenient time for your first visit and organise travel and overnight accommodation if needed.

If you have any queries about your appointment please contact:

Ms Heidi Murray-Smith
Institute of Neurology
London
WC1N 3BG

Telephone: 020 3108 2670
Mobile: 07557 393419
E-mail: **Insight46@ucl.ac.uk**

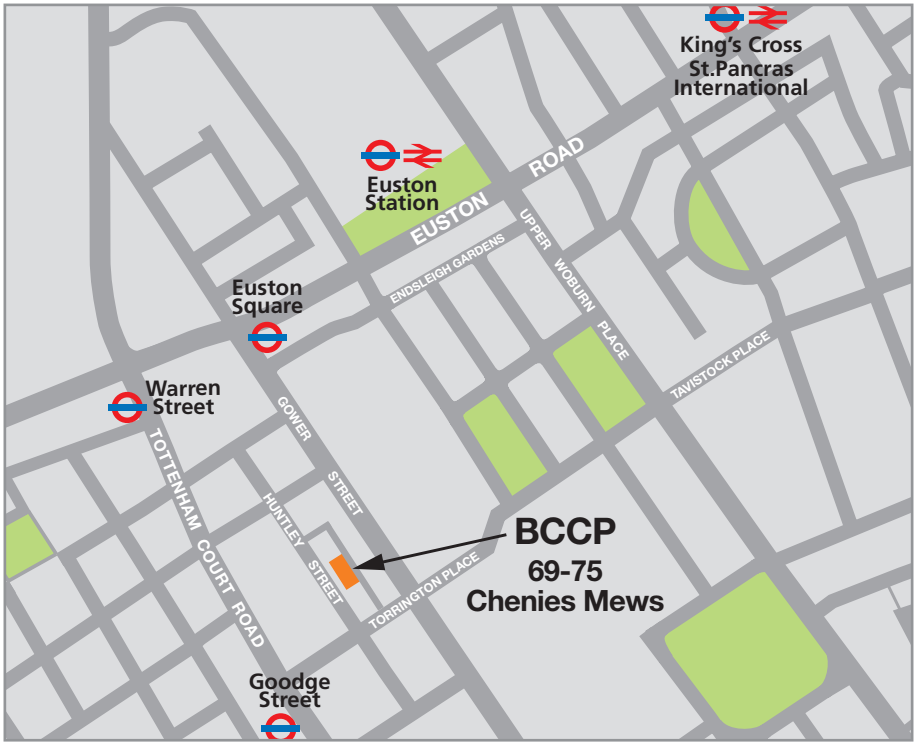
If you have any queries about the NSHD please contact:

Dr Andrew Wong
MRC National Survey of Health and Development
MRC Unit for Lifelong Health and Ageing
1–19 Torrington Place
London
WC1E 7HB

Telephone: 020 7670 5700
Fax: 020 7580 1501
E-mail: **andrew.wong@ucl.ac.uk**
Web: **www.nshd.mrc.ac.uk**

Location of the Bloomsbury Centre for Clinical Phenotyping

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



v4.2_20210510

Nearest tube stations are Goodge 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.

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

MRC Unit for Lifelong Health and Ageing

UCL

National Survey of Health and Development, 2017