Participant Information Sheet

Project Title:

MOTION study – **M**icrobiome **O**f the ageing gut and its effect on human gut health and cogni**TION**.

Invitation:

We invite you to take part in the MOTION study, a research project currently being launched by Quadram Institute Bioscience (QIB), the Norfolk & Norwich University Hospital (NNUH), James Paget Hospital (JPH) and the Norfolk & Suffolk Foundation Trust (NSFT).

Before you decide whether or not to take part, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully, discuss it with others if you wish, and feel free to ask us if there is anything that is not clear or if you would like more information. It is entirely up to you to decide whether or not to take part and, rest assured, whatever you choose, it will not affect the care you receive.

What is the purpose of the study?

All of us have trillions of bacteria and other beneficial microbes in our guts. Collectively they are called the 'microbiome' and they play a critical role in protecting our health throughout our lives. They help us with digesting our food and even with training our immune systems so that we can fight off infections.

This study will help us understand how the gut microbiome changes as we age and how these changes might contribute to, or prevent, age-related conditions in our brain that lead to problems with memory, reasoning or thinking. We call this mild cognitive impairment (MCI).

This knowledge will help us develop new strategies to prevent or delay age-related diseases and maintain good mental health into old age.

We need your help to achieve this, and sincerely hope that you will consider taking part.

Why have I been chosen?

We hope to recruit 360 participants who are at least 60 years old. This is why you will have received information about the MOTION study through your GP, the Bowel Cancer Screening Programme (BCSP), the Norfolk and Suffolk Foundation Trust (NSFT), or if you registered your interest voluntarily.

To join in you will need to fulfil our Inclusion Criteria detailed below. If the Exclusion Criteria apply then, unfortunately, you will not be able to join in, and, if they develop during the study, you may have to withdraw but please read the details below.

Inclusion criteria:

To take part in the study you must:
Be at least 60 years old
Be able to understand the study and provide informed consent
Be able to provide a stool sample within 24 hours of each study visit
Be willing to undergo blood tests at each visit
Be able to complete cognitive tests / questionnaires and be familiar with using an ipad/tablet (support will be available if necessary).

Exclusion criteria:

Unfortunately, you will not be able to take part in the study if you:	
Will need to withdraw if these develop during the study	are currently taking part in an interventional study (this type of study involves the participant receiving some kind of intervention, such as a new medicine, in order to evaluate it)
	are living with or related to any member of the research team
	have a diagnosis of - dementia - Parkinson's disease - Alzheimer's disease - Creutzfeldt-Jakob disease (CJD) - Picks disease - schizophrenia - bipolar disorder - obsessive compulsive disorder - epilepsy
	have had a stroke
	have current, untreated clinical depression
	have an irreversible brain injury
May need to withdraw if these develop during the study	take more than a daily dose of probiotics
	have cancer currently, or history of cancer in the last 5 years, except for squamous or basal cell carcinomas of the skin that have been medically managed by local excision
	have a long-standing gastrointestinal or liver function abnormality requiring on-going medical management or medication
	have made any major changes to your diet in the last month (for example changed to a vegan/ vegetarian diet or stopped eating red meat)
	have a history of any liver problems, for example hepatitis B or hepatitis C
	have a history of alcohol, drug or substance abuse
	have had major surgery of the gastrointestinal tract, apart from gall bladder or appendix removal in the past five years
	have had any major bowel surgery at any time
	have a history of an inflamed bowel, for example ulcerative colitis, Crohn's disease or diverticulitis
	unknown cause; *Clostridium difficile* infection (recurrent) or *Helicobacter pylori* infection (untreated)
	suffer with constipation
	regularly use laxatives
	has an electronic medical implant (e.g. a pacemaker)

Do I have to take part?

No. It is entirely up to you to decide whether or not to take part. If you do, you will be asked to sign a consent form and be provided with all the information you need to take part. You are free to withdraw at any time and without giving a reason. If you do decide to withdraw, you will not be penalised in any way.

What do I have to do if I take part?

Telephone contact

Once we receive an expression of interest from you we will phone you to discuss the study informally, confirm that you are eligible and answer any questions you might have. This usually takes about 20 minutes.

Consenting and eligibility check (pre-study visit)

We will then arrange an appointment to meet you face to face to run through the study with you. This gives us the opportunity to explain exactly how to collect the samples and you the chance to ask any more questions you might have and make an informed choice about whether to continue. If you have been seen by the specialist clinical team at the NSFT with mild memory problems in the past, this team will arrange your appointment at your home. For all other participants, the research team will arrange this

appointment and it will be held at the Quadram Institute Clinical Research Facility. This appointment usually lasts approximately 1 hour.

If you decide to continue, we will ask you to complete the consent form and give you your first sample collection pack. A copy of your consent form will be sent to your GP and to the NNUH with a copy of this MOTION Study Participant Information Sheet to be inserted into your personal medical records. You will also be given a copy of the consent form to keep.

Once you have consented to take part in the study, we will ask you to complete a cognitive test and a questionnaire which is the final eligibility check for taking part in the study. We will let you know in approximately 5-10 days whether your scores are in the required ranges to take part in the study and to arrange your next appointment. These scores are NOT indicative of any clinical diagnosis and are purely for the purposes of the study.

Study visits

Once you are enrolled, we will ask you to attend nine study visits at the Quadram Institute Clinical Research Facility, one every 6 months (+/- 1 month) over the course of the study (approximately 4 years [49 months]). At each of these visits we will take some physical measurements, cognitive assessments, questionnaires, a blood sample, and collect a stool sample from you that you will have collected at home within the previous 24 hours.

We will also ask you to attend three appointments (after 0, 24, 48 months) at Beccles hospital to have pictures and measurements taken of your retina and its blood supply. These are OCT/ OCTA scans (optical coherence tomography/ optical coherence tomography angiography scans).

Some participants will be assigned to subgroups within the study. Not all participants will be asked to take part in these two sub groups but you may be asked to participate in one or both. Participation in these subgroups is completely optional.

Subgroup 1 – colon biopsies (optional) – if you are already on the BCSP and undergo a colonoscopy as part of your routine care, we would like to collect some additional research biopsies (6-8 small 3mm x 3mm x 3mm pieces) at the time of your colonoscopy, so that we can examine the types of cells that attach to the lining of your bowel.

Subgroup 2 – brain MRI (optional) – 30 participants will be offered a brain MRI scan at two timepoints during the study (at 0 and 48 months)

An overview of each of the study visits is shown in the table below:

	Tests	Consent/ Eligibility	Baseline (0 months)	6 months	12 months	18 months	24 months	30 months	36 months	42 months	48 months	Location	Duration
All participants	Cognitive assessments	✓	✓	✓		✓		✓		✓		QIB	45 minutes - 2 hours
	Health questionnaires		✓	✓	✓	✓	✓	✓	✓	✓	✓		
	Stool sample		✓	✓	✓	✓	✓	✓	✓	✓	✓		
	Blood sample(s)		✓	✓	✓	✓	✓	✓	✓	✓	✓		
	Physical measurements		✓		✓		✓		✓		✓		
	OCT/OCTA scans		✓				✓				✓	Beccles Hospital	2-3 hours
Subgroup 2 (optional)	MRI (30 participants)		✓								✓	NNUH	1 hour
Subgroup 1 (optional)	Colon biopsies	Throughout study if given a colonoscopy as part of routine care											As routine appointment

We will provide you with all the information and equipment necessary to enable you to provide any samples required or have any tests done during the study. Travel costs (mileage and parking costs) will be

reimbursed for all study visits if they are not part of your routine care. We will send you reminders for each appointment.

We will also write to your GP at the end of the study to request some routine data from them that they will have collected from you over time. These data are called an electronic Frailty Index (eFI).

During the study, you may be invited to provide an audio/video recording of your experience of taking part in the study. This material will be used to promote public awareness of the study. We may also ask you to provide anonymised quotes for use in research reports and publications. This is completely optional.

CORONAVIRUS UPDATE:

To increase safety during the COVID-19 pandemic, we are implementing the following changes to the way we conduct our study visits at the Quadram Institute Clinical Research Facility:

You should not attend your appointment if you can answer yes to any of the following questions:

- Have you been advised that you are extremely vulnerable from COVID-19 and are therefore shielding?
- Have you or has anyone in your house hold received a positive test for COVID-19, or awaiting results of a test?
- Have you or has anyone in your household had any of the symptoms of coronavirus in the last 14 days? (a high temperature, a new continuous cough, a loss or change to your sense of smell or taste)
- Are you or is anyone in your household self-isolating as a result of the NHS test and trace programme?

We will contact you via telephone to ask these questions within 7 days of your appointment. We will also send you this in a reminder via email or text message the day before your appointment.

We will disinfect surfaces you are likely to come into contact with at your visit before and after your appointment (chairs, handles, desks etc.).

On arrival to the Quadram Institute Clinical Research Facility you will have your temperature checked, if it is raised, we will need to reschedule your appointment.

Social distancing will be in place wherever possible during appointments. However, it is acknowledged that during your physical measurements and while taking your bloods, this may not be possible. The staff conducting this aspect of your appointment will be NHS employees and will be adhering to the latest NHS guidelines on how to conduct this aspect of the study safely.

It is important to note that any participant who does not feel comfortable attending their appointments with these safety measures in place should not feel obliged to, we are happy to reschedule. Please just let the research team know.

What are these tests and why are we asking for them?

In the table below, we describe in detail the scientific reasons why each of the different samples we are asking you to take are so important for our research.

Test	Why are we asking for this test from you?
Stool sample	This sample will be used to compare the numbers and types of microbes in your gut and how they change over time. You will be provided with everything you need to collect this sample including instructions. The samples should be taken within 24 hours of each study visit to QIB, and brought with you when you attend.
Cognitive assessments	Cognitive tests are used to look at your memory, reasoning and thinking. Most of these tests are also used in hospital settings to diagnose levels of cognitive function. Any results we collect from you will not be indicative of any clinical diagnosis and will be used only for the purposes of this research study. There are nine different cognitive tests which the study team will show you before you agree to take part in the study.
Health questionnaires	This questionnaire asks you about your diet, lifestyle and any medications you are taking (including antibiotics). This is so we can relate this to any changes in the microbe populations we find in your samples over time.
Blood samples (15/40mL volumes)	These samples will be used to look for proteins that are indicative of the health of key organs such as the heart, bones, liver and kidneys. We will also be using these samples to run other commonly used tests that measure overall health including Full Blood Count's (FBC), Biochemistry and Troponin I. As an example of how they help evaluate someone's overall health, looking at your red blood cells allows us to detect things like anaemia, while looking at white blood cells help us detect infection. These tests will only be used to measure the number of these cells or the quantity of protein and not to diagnose any condition.
Physical measurements	We will collect some physical measurements of your height and body composition. We will also record your blood pressure (BP) and your hand grip strength (measured using a special instrument that you hold in your hand and squeeze).These will provide information about your general health and physical fitness and will enable us to determine whether any attributes of health and physical fitness are associated with particular changes in cognitive function, vision and/or gut microbe populations.
OCT/OCTA scans	The retina, in your eye, is one part of the body that shows early signs of ageing. These scans look at your retina and the blood supply to it by taking pictures and measurements. For this, you would need to attend Beccles Hospital to see an ophthalmologist (eye specialist). This is a non-invasive and painless procedure which is very similar to having a routine eye test. You may have blurred vision for about 3 hours following this test so will need someone to accompany you and take you home. Further information will be provided before your appointment. Free car parking is available and travel expenses will be reimbursed.
Colon biopsies (optional)	If, while participating in the study, you are asked to have a colonoscopy as part of the Bowel Cancer Screening Programme's routine clinical care, and your doctor decides to take some biopsies as part of this routine care, we would like to collect additional tissue biopsies of your colon at the same time so that we can look at the types of cells that attach themselves to the lining of your bowel. We would request 6-8 very small tissue biopsies in total for this research, each measuring 3mm by 3mm by 3mm. This is completely optional.
MRI (optional)	During the study, we will offer 30 participants a brain MRI scan at the beginning and end of the study. This is not indicative of any diagnosis and is purely for the purposes of this research study. We will relate all the data and samples we collect from you to the MRI scans to see whether they are related to changes in the structure and organisation of the brain over time. This scan is completely optional.
Electronic frailty index	We will write to your GP at the end of the study to request some routine data that they will have collected from you over time. This is called the eFI (electronic Frailty Index). We will use this anonymised data to see whether there are any links between eFI scores and the samples and data we have collected over the course of the study.
Some of the donated samples will be used to better understand how your genes influence the numbers and different types of bacteria that you have in your gut. All types of analyses done using the donated samples, including genetic analyses, have no clinical relevance to you or your relatives and will not affect the treatment you receive. You will not receive a copy of any of these test results but we will send a copy to your GP for their information.	
If you are able to, please bring with you a list of all your current medication/antibiotics to each of your study visits to QIB or Beccles Hospital.	

What happens if something is found during the OCT scan, blood sample, brain MRI scan, or colonoscopy?

If something is found as a result of these tests you may still be able to continue in the study if you wish. If you need to be referred for Specialist Consultant Care and it is not possible for you to continue, we will unfortunately need to withdraw you from the study. We will send you a withdrawal letter and a copy will be sent to your GP. We will keep any data and samples we have already collected from you.

Are there any benefits to taking part?

There are no direct benefits to taking part in the study, but by taking part you will be contributing to important information that will help us better understand how our gut microbiome can influence our health and cognition as we age.

Will my GP be informed?

Yes, it is routine practice for us to inform your GP that you are participating in a study at QIB. We will send your GP copies of all the tests we do as part of this study. You can discuss your results with your GP if you have any concerns.

Are there any risks or side effects from participating in this study?

There can be a small amount of discomfort associated with taking blood. The doctor or nurse will discuss any risks associated with having a colonoscopy and any biopsies prior to consenting you for the procedure.

Do I get paid for doing this?

Participating in this study is entirely voluntary. However, we do recognise that taking part may cause you some inconvenience. As a thank you for participating in the study, a 'Love-To-Shop' voucher to the value of £10 will be posted to your home address after study visit 4 and £15 at the end of the study as a contribution towards your time and any inconvenience.

Mileage to the Quadram Institute Clinical Research Facility (QICRF), NNUH and Beccles Hospital along with any car parking charges will all be reimbursed. Taxi and public transport fares will be reimbursed upon production of a valid receipt.

What happens when the research study ends?

Findings of this study will be reported in the scientific literature. No individual's data will be identifiable.

What will happen to my samples?

All data and samples will be anonymised. Samples will be stored securely at QIB or, if you provide your consent, we will store your samples securely in the Norwich Research Park Biorepository where they may be used for future ethically-approved research after the MOTION study has finished.

What if relevant new information becomes available or changes to the study are made?

If this happens, we will tell you. If changes to the study are necessary we may need to ask you to sign another consent form.

Will I be told the results of the study?

At the end of the study, we will provide you with feedback about what we have found as a result of your help and what it may mean for future research. We will regularly update our websites to fill you in on all the exciting research that we have done using your samples.

The results of the study will also be published in scientific journals and presented at national and international scientific meetings. We are unable to tell you any of your individual results since it is only possible to draw conclusions from the group as a whole.

What if there is a problem, or I would like to make a complaint?

If you have a concern about any aspect of the study, you should ask to speak to a member of the research team by calling 07876182564 or via email on motion@quadram.ac.uk. If you remain unhappy and wish to complain formally, you can do this through Dr Antonietta Melchini, the chairperson of the Human Research Governance Committee (HRGC) at QIB: antonietta.melchini@quadram.ac.uk; 01603 255030.

If you wish to complain or have any concerns about the way you have been treated whilst taking part in this study at the NNUH clinics, there will be a local hospital complaints procedure that you can follow. The PALS (Patient Advice and Liaison Service) is a confidential service designed to support patients, relatives and carers. Their website is pals@nnuh.nhs.uk and the office has an answerphone which is available 24 hours a day: 01603 289036 or 01603 289045.

We are always looking for ways to improve the participant experience in these studies. If you wish to provide any anonymous feedback to the study team you can do so by using this link https://www.surveymonkey.co.uk/r/MOTIONfeedback. The research team will not be able to see who posted these comments so will not be able to respond directly but will certainly take your thoughts on board.

If something happens to me, will I receive compensation?

QIB accepts responsibility for completing trials and, as such, will consider claims from participants for any harm suffered by them as a result of participating in the trial, with the exception of those claims arising from negligence by the participant. QIB has liability insurance in respect of research work involving human participants.

However, if you are harmed as a result of taking part in this research project there are no special compensation arrangements. If you are harmed due to someone's negligence, you may have grounds for legal action, but you may have to pay for it. Please note that QIB will not fund any legal costs arising from any action unless awarded by a court.

How will we use information about you?

QIB is the sponsor and data controller for this study and therefore responsible for looking after your information, using it properly and keeping it confidential.

We will need to use information from you, from your medical records and your GP for this research project.

This information will include your:

- Name/initials.
- Contact details.
- Date of birth.
- Physical measurements collected as a part of the study visits (height, body composition, blood pressure, hand grip strength).
- General health, lifestyle and dietary information. This will be gathered from your answers to the questionnaires we will ask you to complete as part of the study.
- Your responses to the cognitive tests conducted during the study visits.
- Data we will produce from the samples that you provide us.
- Clinical test data (Eye scans, optional MRI scan).
- Electronic Frailty Index Data – A tool used by GPs to identify and score frailty based on routine interactions with their GP.

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name 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.

We will keep your information in a secure archive for 15 years after the study has ended, after which it will be disposed of securely.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study by providing your consent to store your samples in the NRP Biorepository.

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/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to our data protection officer: dpo@nbi.ac.uk, or
- by ringing us on 07876182564.

Who has reviewed this study?

To protect your safety, rights, wellbeing and dignity the study has been reviewed and agreed by the QIB Human Research Governance Committee (HRGC) and an independent group called the Research Ethics Committee (REC) which is made up of expert and lay members.

RECs review research proposals and give an opinion about whether the research is ethical. They also look at issues such as participant involvement in the research. The committees are entirely independent of research sponsors (the organisations responsible for the management and conduct of the research), funders and the researchers themselves. This enables them to put participants at the centre of their review.

What should I do now?

If you are interested in taking part in the study and would like to know more, please go to the study website https://quadram.ac.uk/motionstudy/ and complete the expression of interest form. If you would prefer to speak to someone in the first instance, or require a copy in larger print, then please contact the research team on 07876182564 or email motion@quadram.ac.uk.

If you are not interested in taking part in the study or you are not eligible, you need not do anything. No one will contact you further about the study.

Thank you for taking the time to read this information.