UNIVERSITY OF CAMBRIDGE Cambridge University Hospitals NHS Foundation Trust

Metabolic Research Laboratories, Level 4, Institute of Metabolic Science
Box 289, Addenbrooke's Hospital, Cambridge, CB2 0QQ

Title: Investigating gut hormone levels in human health and disease "GutHHD"

MRI Motility Study

Information Sheet for Volunteers

Many thanks for your interest in this study – this information sheet will explain the study and go through some frequently asked questions.

The study details how we wish to recruit volunteers to have MRIs performed before and after a meal, with combined blood sampling before and after the meal.
You may have been invited to take part in this protocol on its own, or in combination with another GutHHD protocol.

SECTION 1: AIMS OF THE RESEARCH

Who are we and what do we do?

We are a team of doctors and nurses in Cambridge. We are interested in understanding how hormone levels released from the gut vary across different individuals and different gastrointestinal conditions. In particular we are interested in how gut hormone profiles vary in people with regular bowel habits, and how they differ in volunteers with faster and slower moving guts.

What is the purpose of the MRI alongside the meal study?

We wish to understand more how gut hormones effect the speed at which things move through the gut.
MRI (Magnetic resonance imaging) will be used to take images before and after your meal – these are then analysed with software to assess how much and which parts of your gut are contracting, and how fluid moves through the gut. Pairing this analysis with gut hormone

measurements from blood samples, we believe will be a novel method for studying gut hormones and how they affect the gut.

Am I eligible to take part?

You are eligible to take part if you are aged between 18 and 70, and are safe to have a MRI.
MRI imaging involves powerful magnets, and previous surgery involving metalwork, injuries with metal and certain medical devices can make you unsuitable to undergo a MRI.
Every participant will have to undergo a MRI safe checklist to take part.
The study is recruiting a wide range of participants including volunteers with and without a gastrointestinal condition.

Do I have to take part?

Taking part in this part of the study is entirely voluntary. You can take some time to decide whether or not you want to take part and you are free to withdraw at any time, without giving a reason. If you participate, we will ask you to sign a consent form and you will be given a copy of the form. If you do not wish to take part it will not affect the standard of care you receive regularly.

What will happen to me if I take part?

You will be invited to either visit the research facility, or have invitation to a video call conference to have a pre-assessment, answer any questions you have and go through the consent form and MRI checklist.
On arrival for your study day, you will be asked to get changed, and remove any jewellery. Some body measurements will be taken, and a cannula inserted for the blood sampling.
If you are taking part in GutHHD protocol A, this study can be combined with your research day. In this case, you will initially start on the research ward and shortly before the meal portion of the study you will move to the area with the MRI scanner, and then follow this protocol.
Before receiving the liquid meal, for a period of time you will be in the MRI scanner for baseline images to be taken. You will then receive the meal with a drink of water, and then for up to 90 mins after the meal you will spend time in and out of the MRI scanner, for subsequent images to be taken alongside post meal blood samples.

Your blood samples may extend further beyond 90 mins beyond the meal, as per your protocol, and your clinical researcher will explain your blood sampling timeline to you before starting the study.

We will also invite some participants back for a repeat of the visit, with MRI and blood sampling before and after a meal – this will be optional and not compulsory to taking part in a single visit.

Inclusion/Exclusion criteria

We are recruiting a wide range of participants into this study.

You are eligible if you are aged between 18 and 75 and are safe to have a MRI scan.

If you have any permanent medical devices attached to you, and any previous surgery or injury involving metal work, please discuss these with your clinical researcher, as you may not be eligible to have an MRI scan.

Exclusion criteria:

- Known to be pregnant
- Does not pass pre-MRI safety checklist
- Known significant anaemia

Is it safe for me to have an MRI scan? What is it like having an MRI scan?

An MRI scan uses powerful magnets to generate an image of our body, and is capable of producing very detailed images. Unlike other types of imaging such as X-ray or CT scan, it does not involve radiation. MRIs are safe, provided you met the MRI safe checklist, which screen for any medical devices or metalwork in your body which would pose a risk with the magnets. During an MRI scan, you need to stay still for the best possible images to be taken. They can produce a loud noises, but we will provide you with ear protection.

If you are claustrophobic (fear of enclosed spaces) you may find the MRI scan triggering, as it involves staying still in an enclosed tube. Each set of scans will aim to last about 15 minutes, and you will be provided a button to press if you wish to immediately leave the tube during the scan – (note this will likely however make the images taken unsuitable for analysis).

Visit Protocol

- The MRI portion of your study will take place in the **Wolfson Brain Imaging Centre, Cambridge University Hospitals.**
    - You will either be asked to report to the Cambridge Clinical Research Centre, or the Wolfson Brain imaging Centre for the start of your study date.
- **You will need to complete a formal consent form to take part in the study.**
- You will have an in-person or virtual (video or telephone call) pre-assessment prior to the visit, to explain the study, go through any questions, go through the initial MRI checklist and have a brief medical history alongside any medications you are taken recorded.
- **You will need to attend the visit having not eaten or had any calorie or caffeine containing drinks since midnight. Water is OK until 1 hour before the visit starts.**
    - You will also be advised on a standard pasta meal to have the night before your meal.
- You will be asked to change into a hospital gown on arrival and remove any jewellery and a further MRI checklist performed.
- You will have body measurements taken including height, weight, waist circumference and hip measurements.
- Before or after the study you will be given some questionnaires to perform which will ask questions regarding your mood, anxiety, eating behaviour and measures of impulsivity.
    - Some of these questions can raise sensitive topics– if you have any distress or wish to discuss anything further you can discuss this with the study psychiatrist (Prof Paul Fletcher)

- During the study you will be asked some questions regarding how full you feel and feelings within your gut and a questionnaire on your day to day gut symptoms.
- You may also be provided some questionnaires regarding your hunger and fullness and to mark this on a scale throughout the study.
- You will have blood samples collected at the times in your protocol with the meal (up to as frequently as -15, 0, 15, 30, 45, 60, 75, 90 and 120 mins post meal (number of time points will be confirmed to you on the day).
    - The amount of blood taken at each MRI visit will be less than 125ml.

- If you have not had a recent health screening blood test one will be sent to the hospital NHS lab.
    - This will include a full blood count, kidney function, liver function, thyroid function and diabetes screen. These results will be sent to your GP.
- The meal that will be provided will be a set quantity of a liquid meal of Ensure or Fortisip, or an oral glucose drink, with an additional drink of water.
    - Before your visit, your researcher will confirm to you the planned liquid meal being provided and quantity. You will be encouraged to consume all of the liquid meal and water provided, within a period of a few minutes.
- You will have a baseline scan in the MRI scan before the meal, and subsequent scans in-between some of your blood samples. Between scans you will be in the area of the MRI scanner, but do not have to remain in the scanner itself.
- Each scan will last about 15 minutes, but this can vary, and the arrangement for sampling and scans post meal will be explained to you prior to starting.
- You will also be asked to complete a bowel habit diary of at least 7 days including the day of your visit.
- If you are taking part in **GutHHD Protocol A** in combination with the MRI scan:
    - You will have your initial fasting blood samples taken as per protocol A and transfer to this MRI scanner just before your planned meal.
    - You will then have MRI scans as above with your planned pre and post meal blood samples.

Optional second visit

We will invite some participants back for a second visit, at least 7 days after their first MRI scan (no set time for second visit).

It will be optional if you would like to attend for a second MRI scan with blood sampling, and this will be an additional box on the consent form.

The reason for the second visit is because this is a new protocol and additional data is acquired to explore and validate this research method.

At the second visit you may be offered a different meal, and/or different quantity of the meal and water to your first visit. The meal type and quantity will be confirmed before the start of

your second visit. Otherwise it will follow the same design of MRI and blood sample before a meal, and further MRI imaging and blood sampling up to 2 hours after the meal.

Additionally if you are due to start on a new medication and/or treatment that can affect your speed of gut motility (eg treatment for an ongoing bowel condition, surgery, or starting a glp-1 containing treatment such as liraglutide (eg Victoza), semaglutide (eg Wegovy/Ozempic) or tirzepatide (eg Mounjaro)) we may invite you for a second visit after starting your new treatment, to assess if any change to your gut motility and/or gut hormones and metabolic markers has occurred.

What if I am taking a medication that effects gut transit (such as loperamide, ondansetron, codeine, bile acid sequestrants).

This will depend on the medication.

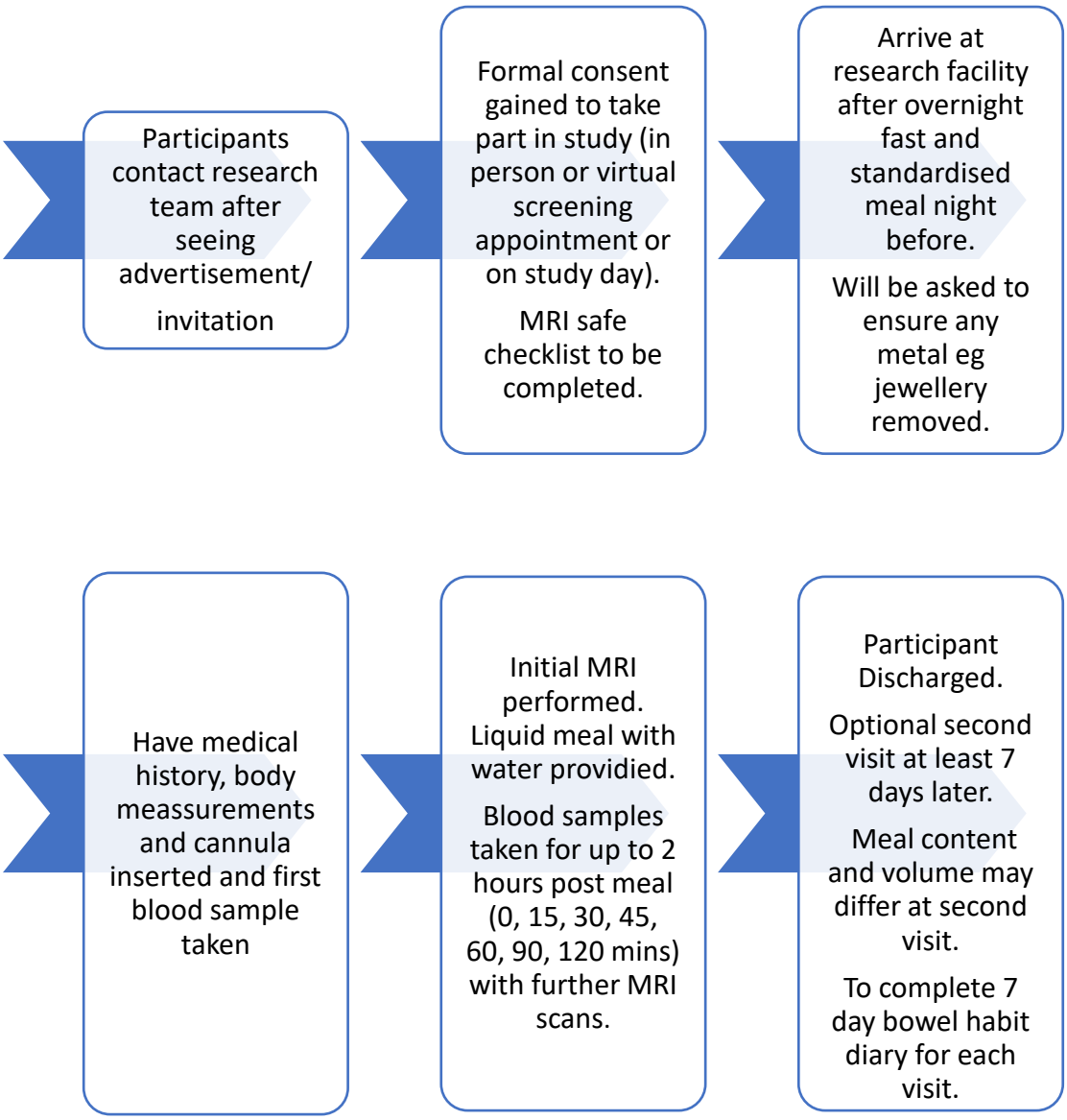
If you take loperamide, ondansetron or codeine (or other opioids) you will be asked to avoid these medications for 24 hours prior to the study if possible. That is because these medications can slow down gut transit and it is unknown how they would affect the results.

If you cannot avoid these medications for 24 hours, discuss this with your researcher; you may still be able to take part at the investigator's discretion and decision.

If you take bile acid sequestrants you will have different options. You can either:

- Take as normal up to the visit.
- Pause for 72 hours prior to the scan
- Potentially attend for two visits, one visit taking your sequestrants as normal, and the other visit pausing sequestrants for 72 hours prior to the visit.

<u>Diagram of research day:</u>



What will happen to my data collected in the MRI scan and my blood samples?

If you agree to take part in the study you will complete a formal consent form.

Your research images, samples and data will be given a unique anonymized research ID. Only clinical researchers named on this project (***Dr Chris Bannon, Dr Htar Htar Hlaing, Prof Fiona Gribble, Dr Jeremy Woodward, Dr Phillip Wild, Dr Agatha Van der Klaauw and Prof Paul Fletcher***) will have access to the identity of the samples and images, and to all other processing the data they will only see a unique research ID.

MRI Data

Your MRI will be stored with your identifying data on a secure clinical server as part of Cambridge University Hospitals. Scans are not routinely reported on by a radiologist to assess for any abnormalities. MRIs produce very detailed images and can show abnormalities within the body you were not aware of. If there is a clear abnormality seen during the study, your scan may be referred to a radiologist to have a formal report, but scans taken for research purposes will not be routinely examined by a radiologist. If relevant to your clinical care at a later date, your scan has the option of being sent to your regular doctor.

For the purposes of research within the study, your scan data will have any identifying information removed, and will only have your research ID. The de-identified data will then be uploaded to the secure servers of our collaborators Motilent for the duration of this component of the study and analysis (until latest March 2026) and then will be deleted (https://www.motilent.io/contact).

Motilent is a commercial company that provides novel software for analyzing movements of your gut – and we will be using this data to pair to your blood results. Motilent regularly provide analysis of clinical images for research and clinical care, and the data sent to their servers will be anonymized.

Blood samples:

If you have some health screen blood tests performed, these will be standard tests used in hospitals and general practice, including your full blood count, kidney function, liver function tests, lipids, markers of glucose metabolism and thyroid function. These will be processed in the regular clinical laboratories at **Addenbrooke's** Hospital and, as they are performed in a regular NHS laboratory, the results will be added to your medical records.

Other tests will be more specialized and more common to research rather than regular clinical use and will include gut hormones and other metabolic markers.

The blood samples you provide for these purposes will immediately be processed to remove any cells and genetic material. The remainder of the blood sample will then be frozen and stored initially at the University of Cambridge. Your samples will be given a unique anonymized research ID.

The majority of analysis will take place in the University of Cambridge and University of Cambridge Hospitals laboratories, **however it may be necessary for specialized tests that your samples need to be analyzed at another collaborator NHS or University laboratory.**

What are the possible benefits of taking part?

This research study is aimed at advancing knowledge only and may not result in any direct medical benefit to you or specific patients.
It will help us to learn more about how different gut hormone levels and metabolic markers vary after a meal, and how their levels influence gut movements, gut motility and the speed at which things move through our gut.

What if some of the tests show that I have a particular problem?

If any of the tests show anything that might require further medical assessment, these results will be discussed with you and appropriate follow-up will be arranged through the doctor at your local hospital or your GP.

Can I claim back travel expenses?

You can claim back up to £50 travel expenses per visit for attending the visit, and a £50 participation fee for taking part in the study itself.

Can I withdraw from the study?

You can withdraw from the study at any time without giving a reason. You will be asked if you wish for your research data and samples collected to that point to remain in the study or if you would like them to be removed from the study.
If you wish to withdraw from the study, before the visit this can be done via email to the research team (email: **cuh.guthormones@nhs.net**).

On the study day this can be performed verbally to one of the research nurses or research doctors and this will be documented and a withdrawal form provided to you. If you wish to withdrawal after the study day, this can be done by contacting the research team by email or by post (**email cuh.guthormones@nhs.net**).
A withdrawal form will be provided to sign to state if you would like your data and or samples additionally removed as well. If a form is not returned but you have stated in writing you wish for samples and data to be removed this will be acted upon.

Will my taking part in the study be kept confidential?

Yes. All information collected will be anonymised and kept confidential and be kept separate from your medical records; any information which can identify you, for example your name

and address, will not be revealed. Anonymous data will be stored on both paper and electronic format and can only be traced back to you with a coded crib sheet.

This crib sheet encoding your identity to your research id will be stored on paper in a locked file cabinet in the Institute of Metabolic Science, and electronically on an encrypted spreadsheet kept on Addenbrooke's clinical computer network. Only named clinical researchers **(Dr Chris Bannon, Dr Htar Htar Hlaing, Prof Fiona Gribble, Dr Jeremy Woodward, Dr Phillip Wild, Dr Agatha Van der Klaauw and Prof Paul Fletcher)** will have access to this crib sheet.

Non-anonymised data such as the crib sheet will be kept for up to 3 years after the study has concluded.

Other researchers will only have access to the anonymised data which will be stored electronically and on paper. Anonymised data will be stored long term after the study and will be used for publication.

To ensure adherence to Good Clinical Practice, our research will be monitored by the NHS Trust; however, all information will remain confidential. Our data management is in compliance with the Data Protection Act.

It is anticipated it will take up to a year to recruit all required volunteers for this part of the study and a further year for the analysis.

Blood samples will be stored after the study for up to 10 years with an anonymous research ID for potential analysis with newer techniques for measuring gut hormones and other metabolic markers in the future. If you wish for your blood samples to be removed please contact the team and they will be removed and destroyed.

After this any remaining blood samples will be disposed of and destroyed.

MRI images will be stored on CUH servers with your identifying details before then being anonymised. Anonymised images will be transferred to Motilent servers for analysis, but will only be stored on their servers for the period of analysis.

Further information on data collection

Cambridge University Hospitals NHS Foundation Trust (CUHNFT) and the University of Cambridge are joint sponsors for this study based in the United Kingdom.

CUHNFT and the University of Cambridge will be using information from you and/or your medical records in order to undertake this study and will act as joint data controllers.

This means that both organisations are responsible for looking after your information and using it properly.

The University of Cambridge will keep identifiable information about you for 3 years after the study has finished.

CUHNFT will keep identifiable information about you for 3 years after the study has finished.

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 using the following links:

For Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/patient-privacy/, or email the Data Protection Officer at: cuh.gdpr@nhs.net

For University of Cambridge, please visit: https://www.information-compliance.admin.cam.ac.uk/data-protection/medical-research-participant-data,, or email the Information Governance team at: research_governance@medschl.cam.ac.uk

https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/transparency-wording-for-all-sponsors/

Will my doctor be informed?

Should you decide to take part in this study, with your agreement, your GP will be informed of your involvement.

Will my medical notes be accessed by the research team

With your consent your medical notes will only be accessed by a clinical researcher on the team. This will be for the purpose of checking your baseline blood results in the study, check previous blood results, past medical history and other test results relevant to the study and to inform your GP if there are any abnormalities, to check you met the inclusion and exclusion criteria and anything else relevant to the study. All aspects will remain anonymised within your research data which are kept separate from your medical notes.

What will happen to the results of the research study?

We also intend to publish the results in relevant medical journals as they are likely to be of considerable benefit to both the scientific and medical community. Nothing that can be

directly traced back to you will be published, everything will be in an anonymised format only.

A copy of the results can be obtained by contacting the research team (cuh.guthormones@nhs.net) with any questions and to obtain a copy of the results when published in scientific journal.

Newly published research will be also published on the IMS-MRL webpage (https://www.mrl.ims.cam.ac.uk/) where results of studies are advertised once published.

What if there is a problem?

If you have a concern about any aspects of this study, you should ask to speak to the clinical team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure.

As a point of reference the Patient Advice and Liaison Service (PALS) service contact details for Addenbrookes hospital are:

Email: cuh.pals@nhs.net

Phone: 01223 216756

The risks of participants suffering harm as a result of taking part in this study are minimal, but insurance (provided by the University of Cambridge and the NHS indemnity scheme) will provide compensation for any negligent harm caused by participation.

Who is funding the research?

The funding for this study comes from a grant to Prof Gribble from Wellcome to measure gut hormones in human blood samples using new techniques. The salary for Dr Bannon working on the trial also comes from this grant.

The MRI portion of the study will have additional funding from Wellcome funding for Prof Paul Fletcher.

Who has reviewed the study

All research in the UK is reviewed by an independent group of people, called a Research Ethics Committee, in order to protect your safety, rights, wellbeing and dignity. This study has been

reviewed and given a favourable opinion by the East of Scotland Research Ethics Service research committee.

Contact details:

Additional information or questions regarding this study can be obtained by contacting the following research team members at the above address and telephone numbers (01223 762634)

- Professor Fiona Gribble
- Doctors: Christopher Bannon (cuh.guthormones@nhs.net) (main contact)

This is the end of the information sheet. We would like thank you for taking the time to read this sheet. If you wish to participate, do let us know.