IMPERIAL

Participant Information Sheet

Optimising Gastrointestinal Hormone and Satiety Responses through Targeted Delivery of Metabolites to the Human Gut

Title	Optimising Gastrointestinal Hormone and Satiety Responses through Targeted Delivery of Metabolites to the Human Gut
Short Title/ Acronym	Gut infusion study
Study Sponsor	Imperial College London
Study Site	NIHR Imperial Clinical Research Facility
Address	6th floor Commonwealth Building Imperial College London Hammersmith Campus Du Cane Road London W12 0NN

IMPERIAL

Contents

1. Invitation to take part in the study.

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others, if you wish. You can talk to family, friends, or a carer about the study. Ask us if there is anything that is not clear or if you would like more information. Thank you for reading this.

2. What is the purpose of this study?

Obesity affects over 1.6 billion people worldwide. Obesity rates in the UK are among the highest in Europe. In England, approximately two in three adults are overweight or obese.

Chickpeas have a positive impact on metabolic health. Our previous research has shown that chickpea intake changes a range of small molecules in the gut, which further leads to the release of gut hormones such as GLP-1 and PYY - hormones that are known to play a role in improving blood sugar control, enhancing satiety and weight loss.

In this study, we will infuse the molecules that are related to chickpea digestion directly to your gut to understand how these molecules can affect your gut hormone and satiety response. This will inform effective dietary strategies to help people manage their weight and health.

3. Why have I been chosen?

This study will involve 15 healthy participants. You have been invited to take part in this study because you possibly meet the following criteria:

•You are aged 18-65 years (inclusive)

•You have a body mass index (BMI) between 18.5-30 kg/m2

•You are able to give written informed consent and, understand what you would need to do to take part in the study.

If any of the following apply to you then unfortunately you are unsuitable to take part in this study:

•Previous surgery on the bones inside the nose, or nasal airway obstruction

•Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome

•Abnormal ECG

• Screening blood results outside of normal reference values

• Weight change of more than 5kg in the preceding 2 months

• Current smokers

• History of substance abuse and/or excess alcohol intake

• Pregnancy

• Diabetes

• Cardiovascular disease

• Cancer

• Kidney disease

• Liver disease

• Pancreatitis

• Started new medication within the last 3 months likely to interfere with energy metabolism, appetite regulation and hormonal balance, including: anti-inflammatory drugs or steroids, antibiotics, androgens, phenytoin, erythromycin or thyroid hormones

• Participation in a research study in the 12-week period prior to entering this study

• Any blood donation within the 12-week period prior to entering this study

4. What will I need to do if I take part in the study?

The study team will contact you by email or telephone if you are interested in taking part in the study. They will tell you details about the study and what you will need to do if you take part.

Registered at ICHNT:
If you decide to undergo the study, you will be registered as a patient at the Imperial College Healthcare NHS Trust. This will not affect the care or treatment you receive in other hospitals.

Pre-screening questionnaire:
You will complete a pre-screening questionnaire. This helps us find out if you can take part in the study. If you decide not to proceed, your pre-screening questionnaire data will not be stored. You will have unlimited time to consider participation before providing consent, and you are free to withdraw from the study at any point without the need to provide a reason.

Screening:
You will attend the NIHR/Wellcome Trust Imperial Clinical Research Facility at Hammersmith Hospital where your eligibility will be assessed. You will have a blood test and height and weight measurements will also be taken. You will have a nostril assessment checked by our research doctor. You will also have an electrocardiogram (ECG) and your blood pressure will be recorded. All women of childbearing age will have a pregnancy test. You will be asked to sign the consent form if you agree to participate in this study. If you change your mind, you can withdraw from the study at any time.

Pre-Visit Guidelines:

On the day before the study visit, we will ask you to refrain from strenuous exercise, caffeine, seeds, and alcohol. You will then be requested to fast overnight from 10 pm (you are allowed to drink water).

Study visit:

You will attend one 3-day (2 nights) inpatient study visits at the NIHR Imperial Clinical Research Facility (W12 0NN). The map and facility contact can be found in https://www.imperial.ac.uk/nihr-crf/contact-us/. During your stay, we will provide all of the food you require. You will be requested to fast every evening of the visit from 10 pm (you are allowed to drink water).

Day 1-2 : Gut Tube Placements

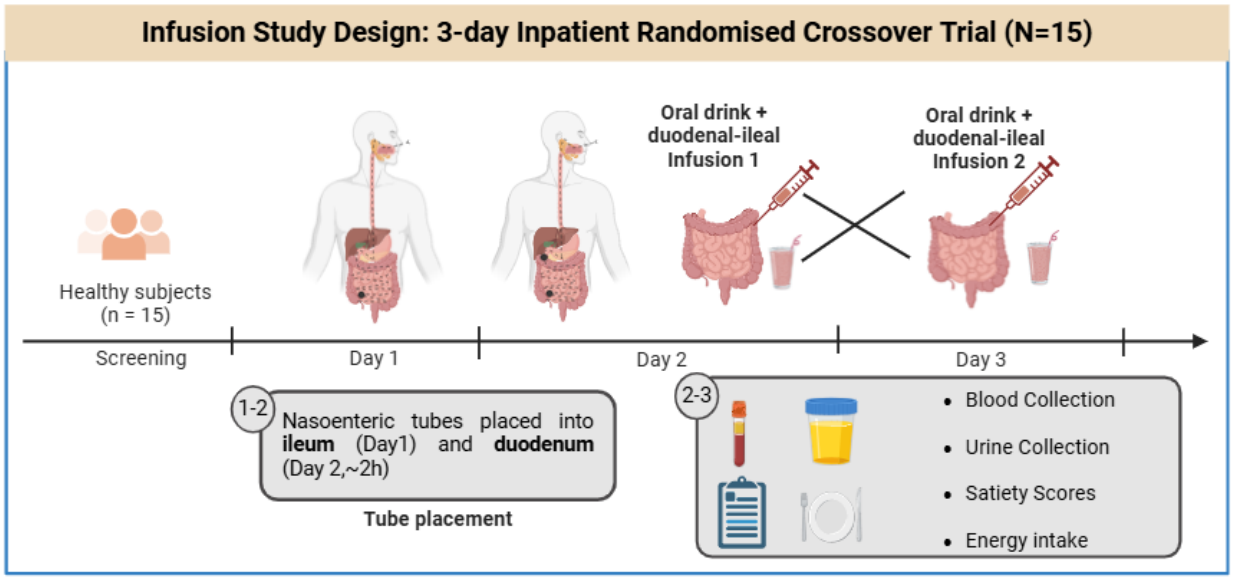
On the the mornings of day 1 and day 2, our trained medical professionals will carefully perform two tube placements into your gut. These tubes will help us deliver nutrients directly to your small intestine so that we can see how your gut responds and how it affects appetite. On day 1, one tube will be placed in your lower part of the small intestine called the ileum; and on day 2, another tube will be placed into your upper part of the small intestine called the duodenum. The tubes will stay in place throughout the 3-day study visit and we will check the positions regularly to ensure they are in correct places.

On day 1, you will be asked to arrive at Charing Cross Hospital by 8:00 am. One tube will be inserted into one region of your small intestine (ileum) via your nostril. The tube will be placed whilst you are awake. It is not painful but can result in a little discomfort which can be minimized with drinks and we will apply local anaesthetic jelly into your nose before tube placement which also help reduce the discomfort. Fluoroscopy is a type of medical imaging that shows a continuous X-ray image on a monitor, much like an X-ray movie. We will check the tube progress using a small dose of fluoroscopy to ensure it is in the right spot. Following insertion of the tube, you will be provided with a light breakfast meal. This will help the tube naturally progress towards the ileum. We will monitor the positions regularly throughout the day to ensure they are in correct places. Once the tube is in place, you will travel via taxi/uber with a researcher to Hammersmith Hospital (about 15-20 minutes). All remaining research activities will take place at Hammersmith Hospital. You will be provided with lunch and dinner from the hospital.

On day 2 in the morning, another soft tube will be placed through your other nostril into another region of your small intestine (duodenum) The tube will be placed by a trained medical professional following similar procedures as in day 1, but it will take less time (usually 5-10 minutes). We will apply some lubricant on the end of the tube to make it slippery and place it through your nose and down into your stomach and then the duodenum. You will be sat initially upright as the tubes are placed and asked to drink water through a straw as this will help the tubes to go down. On the imaging couch we will roll you into different positions to help placement. It will feel a bit uncomfortable whilst the tubes are being put in, however, any discomfort should subside once the tubes have been positioned and you get used to them.

What sizes of the tubes are used: The ileal tube is about 3mm thin and 4 metres long. The duodenal tube is about 4mm thin and 1.5 metres long. Both tubes are made as soft as possible to minimise discomfort. We will show you the tubes on the screening visit and you can feel the texture and look at the tubes. We have a video to show you what a tube insertion looks like.

How do we make sure the tubes are correctly placed? When we place the tubes, we give you a drink of barium sulphate, which allows us to see the 'film' of your bowel clearly under fluoroscopy. The end of the tube has a magnetic tip that can be seen under fluoroscopy so our doctor can monitor the tubes are in the right places. Once the tubes are in place, we will also check the position of the tubes regularly by taking a small amount of intestinal fluid and checking the pH.



A diagram explains the tube placements and study procedures on the main 3-day study visit.

Day 2-3 : Gut Infusion Interventions

On day 2, once the tube placements are checked in the appropriate locations, we will settle you down into a comfortable position to receive the interventions. The interventions include an oral drink followed by gut infusions via the tubes, and the whole procedure will last for 180 minutes. First, you will have a drink with straw, and we will ask you to finish it within 5 minutes. The straw will be positioned at the back of your mouth, so the drink goes directly to your stomach without mixing too much with your saliva. After that, we will deliver specific nutrients/ small molecules into the duodenum and ileum through the tubes. The entire process will take about 180 minutes.

The oral drink and liquids delivered through the tubes are made up of a mixture of nutrients and small molecules from foods- including simple sugars and amino acids (the building blocks of proteins), which your gut normally procedures when you eat meals like peas or beans. The extact ingredients used in the infusions are listed in the Appendix 1 at the end of this document.

During this 180-min period, the following assessments will be completed:

(1) Blood sample collection

You will have a small plastic cannula tube inserted into a vein in one arm. A vein is the type of blood vessel commonly used for taking blood samples. You may feel minor discomfort whilst the cannula is being inserted. After the cannula tube has been inserted this will be used to take blood samples to measure the levels of hormones which control hunger in your body. On day 2 and day 3, approximately 120 ml of blood (~6 tablespoons) will be collected per day. We will take blood samples from you at 14 timepoints and the overall amount of blood we will take per day is 120 ml. We will measure the levels of hormones and small molecules in your blood that influence appetite as well as glucose and insulin levels in your blood.

(2) Appetite scores

After each blood sample is collected, you will be asked to fill in a chart describing how hungry you feel.

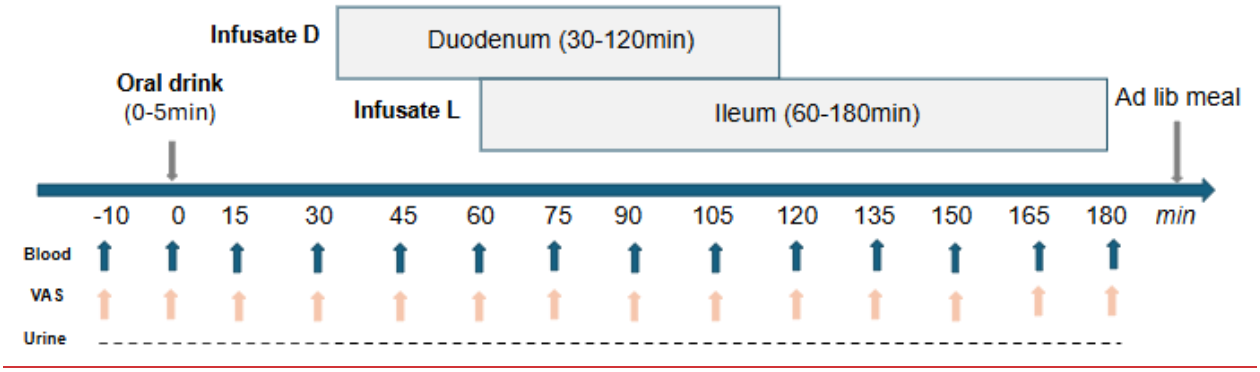
(3) Urine sample collection

Your urine will be collected throughout the 180 minute to measure levels of small molecules related to your appetite. We will provide an appropriate measurement container to collect urine.

(4) Food intake

Immediately after the infusion interventions, you will be provided with a pasta meal and asked to eat as much as you need to feel full. We will measure how much you eat to understand your appetite change.

The diagram below summarises the assessments we will carry out:



Once you complete the pasta lunch on the third study day, the tubes in your small intestines and the plastic cannula will be removed and you will be able to go home. It is expected that the majority of participants will have the naso-enteric tubes removed through the noses at the Clinical Research Facility at Hammersmith Hospital, without the need of fluoroscopy or anaesthetic jelly. If more than mild discomfort seems likely to be caused by the removal of the tube, we will transport you to the Imaging Department at Hammersmith Hospital for removal of the tube under fluoroscopy. Exceptionally, the nasal end of the tube will be cut and the rest of the tube will be allowed to pass rectally.

After study visits:

Your GP will be informed of your participation in this study with your permission. A letter will be sent to your GP through the email you provided in the pre-screening questionnaire.

5. What are we testing?

We are measuring how infusion of nutrient molecules, which were associated with gut hormone release from chickpea digestion change your appetite and food intake. We are also measuring levels of hormones which influence appetite, other markers of glucose, appetite, and metabolism, levels of nutrients in the bloodstream, nutrient molecules, as well as other routine blood tests.

6. Do I have to take part in this research study and what are the alternatives to taking part?

No. You do not have to take part. If you decide to take part and later change your mind, you are free to withdraw from the study at any stage, without giving a reason.

7. What are the possible benefits of taking part?

Taking part in the study will provide no direct benefit for you. The information that we get from this study will help us to better understand how food changes our appetite and may help us to better treat future patients who suffer from obesity. If any of the screening questionnaires or blood tests reveal any medical problems (e.g. diabetes, kidney or liver problems), your GP will be informed so that they can coordinate your further care, arrange any further tests, and refer you on to Hospital Doctors if necessary.

8. What are the side effects of taking part?

The nutrient molecules you will receive are molecules that people would produce naturally after eating chickpeas. They are generally not found to be linked to any serious side effects.

9. What are the possible risks and disadvantages of taking part?

Blood Cannulation	Insertion of the cannula into your arm on each of the study visits may cause minor discomfort or superficial bruising. Serious risks associated with the insertion of the tubes are very rare and almost negligible. These risks include bleeding, perforation or damage to the base of the skull.
Discomfort of Tube Placement:	During tube placement and removal, minor discomfort in the back of the throat occurs in the majority of patients and may result transiently in a sore mouth, thirst, swallowing difficulties, or hoarseness. For most subjects, the discomfort decreases once meals are consumed with the tube in place.
Risks of Tube Misplacements	Tube Slip-Back or Over-Travel: Our team has performed over 90 tube placements and has encountered rare risks. Tube coiling in the intestine: In some cases, the tubes may slip back or coil in the intestine. This would be typically identified during routine tube position checks under fluoroscopy on the morning of day 2 or day 3, before the infusion experiments. If this occurs, the doctor may inflate the balloon at the end of the tube to guide it back to its original position, determined by the pH of collected samples and fluoroscopic confirmation. This process is usually painless. In rarer cases, additional adjustments may be needed to correct coiling. The doctor may gently pull the tube back through the nose to remove the coiling, but if this is coiled you might experience retching or gagging as it is removed. You may experience minor discomfort during this process, similar to what you may feel on day 1. If it is not possible to correct the tube's position, the doctors may decide to remove this tube and discharge you from the hospital. A

	further tube insertion will not be performed in the same visit. Tube over-travel: Once the tubes are in place, the ends will be taped securely around your nose to prevent further movement. Out of our 90 insertions, early on, one participant passed the end of the tube through the anus. In this case, the tube was cut around the nose to allow the rest of the tube to pass rectally. The subject reported no pain or discomfort during this process and was allowed to eat and drink normally, allowing the tube to pass with his bowel movements and was discharged on the same day with no long-term effects. We have established protocols and an experienced medical team at the facility to address any misplacement of tubes, although the likelihood of such events is very low. As we have become more experienced in this technique, tube over-travelling and coiling have become very rare (none in the last 30 placements).
Radiation exposure	If you take part in this study, you will have an Ileal and duodenal tube placement/removal under fluoroscopy. These procedures use ionising radiation to form images of your body and help your doctor position the tubes correctly. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small chance of this happening to you.
Time commitment	If you choose to take part in this study, you will need to stay with us for three days (two nights). The ileal tube placement will take place on the first day, starting at 8 AM. We understand that this is a significant time commitment, and we truly appreciate your participation.

It should be noted that the health screenings performed as part of this study cannot be viewed as a comprehensive health check. However, vary rarely, unexpected observations may be detected which may need further investigation. In this event, you will be informed, and a report will be sent to your GP, who will arrange further tests and coordinate your further care.

10. What if new information arises during this study?

Sometimes during the course of a study, new information becomes available. If this happens, the study team will tell you about it and discuss it with you. If you decide to continue in the study you will be asked to sign an updated consent form. Also, on receiving new information the study team will consider it to be in your best interests to withdraw.

11. What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Insert name and contact details). The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team'

12. What happened when the research study stops?

Once the study has finished, the results of the study can be made available to you should you wish. If you have any problems immediately following the study, then you should contact one of the research team on the numbers provided below.

13. How will we use information about you?

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

1. 10 years after the study has finished in relation to data subject consent forms.
2. 10 years after the study has completed in relation to primary research data.

The study is expected to finish in December 2026. For more information / confirmation regarding the end date please contact the study team, see '**WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED'** for contact information.

We will need to use information from you for this research project. This information will include your

1. Initials
2. NHS number
3. Name
4. Contact details
5. GP details

People within the College and study team (see section **SHARING YOUR INFORMATION WITH OTHERS**) will use this information to do the research or to check your records to make sure that research is being done properly and the information held (such as contact) details is accurate. People who do not need to know who you are will not be able to see your name or contact details.

Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

• Imperial College London - "performance of a task carried out in the public interest"); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies on scientific or historical research purposes or statistical purposes.

INTERNATIONAL TRANSFERS

There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA. Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your personal data is processed.

SHARING YOUR INFORMATION WITH OTHERS

We will only share your personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.

Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

Some anonymised data will be analysed by researchers in the Food Innovation and Health Programme at Quadram Institute Bioscience. The address is Norwich Research Park, Colney Ln, Norwich NR4 7UA. Data and samples to be shared will be pseudonymised before being shared. We have maintained material transfer agreement (MTA) in place to collaborate with Quadram Institute Bioscience.

POTENTIAL USE OF STUDY DATA FOR FUTURE RESEARCH

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

COMMERCIALISATION

Samples and data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure your name and any identifying details will NOT be given to these third parties, instead you will be identified by a unique study number with any sample / data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be created using your data (in a way which does not identify you individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your data will not be shared with a commercial organisation for marketing purposes.

USE OF BLOOD SAMPLES IN FUTURE RESEARCH

All of blood samples will be kept in the Section of Nutrition at Imperial College London and will only be used for other research purposes which have been ethically approved by an NHS REC under Section 1(19) of the Human Tissue Act.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED

1. You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. Because some research using your data may have already taken place and this cannot be undone. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you if this could affect the wider study or the accuracy of data collected.
2. If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED

You can find out more about how we use your information
1. at www.hra.nhs.uk/information-about-patients/
2. by asking one of the research team
3. by sending an email to Dr Mingzhu Cai at m.cai18@imperial.ac.uk or Professor Gary Frost at g.frost@imperial.ac.uk

WHAT IF YOU HAVE GIVEN INFORMED CONSENT, LOSES CAPACITY TO CONSENT DURING THE STUDY

You and your all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.

COMPLAINT

If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to Dr Mingzhu Cai at m.cai18@imperial.ac.uk or Professor Gary Frost at g.frost@imperial.ac.uk

Following our response, if you are not satisfied please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you remain unsatisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO) – via www.ico.org.uk.Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

14. What will happened to the results of the research study?

The results are likely to be published the year following the study completion. Your confidentiality will be ensured at all times, and you will not be identified in any publication. At the end of the study, the results of the study can be made available to you and/or your GP should you wish.

15. Will I be reimbursed for my travel expenses/time?

In recompense for your travel and time during study visits, £500 will be reimbursed once you complete all study procedures. This amount also reflects similar expense payments offered in previous studies by our research group.

If you attend the screening visit but decide not to participate in the main study, your travel expenses for the screening visit can be reimbursed. If you attend but withdraw from the main study visit, you will be compensated on a pro-rata basis. For example, if you withdraw after completing Day 1, you will receive 1/3 of the payment, and after completing Day 2, you will receive 2/3 of the payment.

The researchers will not receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research.

16. Who is organising and funding the study?

This study is being organised by the Section of Nutrition, Department of Metabolism, Digestion and Reproduction, Imperial College London and is being funded by the Biotechnology and Biological Sciences Research Council (BBSRC).

17. Who has reviewed the study?

This study was reviewed by Health Research Authority (HRA). This study was given a favourable ethical opinion for conduct in the NHS by London - Surrey Borders Research Ethics Committee.

18. Further information and who to contact

If you have any questions regarding the study please contact the researcher (Dr Mingzhu Cai) on m.cai18@imperial.ac.uk.The hospital switchboard (020 8383 1000) has home and mobile phone numbers for all the researchers involved in the study and can contact them at any time outside normal working hours. If you agree to take part in the study, you will also be given the contact details of the researchers. If you experience any problems during this study, you may withdraw at any stage.

Thank you for taking the time to read this.

Appendix 1. Ingredients of drink and infusates

Interventions	Oral Drink	Duodenal infusion	Ileal infusion
Timeframe	T0-5 min	T30-120 min	T60-180 min
Formula	Maltose 16.6mM Glucose 4.2mM	Alanine 0.05mM Valine 0.06 mM Glutamine 0.02mM Histidine 0.03mM Asparagine 0.02mM	Maltose 0.83mM Glucose 1.25mM Aspartate 0.10mM Tyrosine 0.11mM Alanine 0.11mM Tryptophan 0.05mM Histidine 0.05mM