

# Investigating how infusing nutrients into the gut affects gut hormones and appetite

<b>Submission date</b> 28/02/2025	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 05/03/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 05/03/2025	<b>Condition category</b> Digestive System	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Obesity rates are rising worldwide, creating an urgent need for safe and effective treatments. Gastrointestinal (GI) hormone-based drugs are emerging as new therapies. The gut contains specialized cells known as enteroendocrine cells (EECs) that release different hormones after meal ingestion. For example, K cells and I cells in the stomach and upper intestines release gastric inhibitory polypeptide (GIP) and cholecystokinin (CCK), respectively, while L cells further down the intestine produce oxyntomodulin (OXM), glucagon-like peptide 1 (GLP-1), and peptide YY (PYY). These hormones send signals to the brain, informing it about the body's energy and nutrient levels, which help regulate food intake. When food is consumed, it is broken down into small molecules (nutrients) that can interact with these hormone-producing cells in the gut. Previous research has shown that the structure of plant foods, such as chickpeas with intact cell walls versus broken cells, can affect which nutrients are present in the gut and how the gut responds. However, it is not yet known which nutrients specifically trigger the production of these hormones and increase feelings of fullness, or where in the gut these signals originate. To explore this, this study will directly infuse nutrients related to chickpea digestion into specific parts of the gut and monitor hormone responses over three hours. By studying these responses, the aim is to identify the key areas of the gut and the nutrients that drive feelings of fullness when digesting legumes. This information could help design plant-based foods that make people feel fuller for longer, supporting weight loss and combating obesity.

### Who can participate?

Healthy adult male and female volunteers aged 18 – 65 years old with a BMI of 18 – 30 kg/m<sup>2</sup>

### What does the study involve?

15 healthy participants will be recruited from the healthy volunteer database. They will attend a screening and a 3-day inpatient study visit at the NIHR Imperial Clinical Research Facility.

### What are the possible benefits and risks of participating?

**Benefits:** Taking part in the study will provide no direct benefit for you. The results 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.

#### Risks:

**Nutrient infusion:** The nutrients infused into your gut are naturally produced in your gut after eating peas or chickpeas. They are generally not found to be linked to any side effects. **Blood cannulation:** Insertion of the cannula into your arms on each of the study visits may cause minor discomfort or superficial bruising. **Risk associated with tube placement:** If you take part in this study, you will have an ileal and duodenal tube placement 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. Everyone is 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. 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. Rare risks were observed associated with Tube Misplacements.

Where is the study run from?

NIHR Imperial Clinical Research Facility, Hammersmith Hospital, UK

When is the study starting and how long is it expected to run for?

January 2023 to January 2028

Who is funding the study?

Biotechnology and Biological Sciences Research Council (BBRSC), UK

Who is the main contact?

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## Contact information

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Public

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## Additional identifiers

**EudraCT/CTIS number**

Nil known

**IRAS number**

349450

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

CPMS 66409, Biotechnology and Biological Sciences Research Council Grant Code BB/X018857/1

## Study information

**Scientific Title**

Optimising gastrointestinal hormone and satiety responses through targeted delivery of metabolites to the human gut

**Study objectives**

Infusion of legume digestion-related nutrients into the stomach, duodenum, and ileum will enhance gut hormone and satiety responses compared to the infusion of saline in healthy subjects.

**Ethics approval required**

Ethics approval required

**Ethics approval(s)**

Approved 25/02/2025, London – Surrey Borders (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)2071048057; [surreyboundaries.rec@hra.nhs.uk](mailto:surreyboundaries.rec@hra.nhs.uk)), ref: 25/LO/0050

**Study design**

Randomized controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Laboratory, Medical and other records, University/medical school/dental school

**Study type(s)**

Other

**Participant information sheet**

See study outputs table

**Health condition(s) or problem(s) studied**

Investigating gut hormone and satiety responses

**Interventions**

15 healthy volunteers will attend a screening and a 3-day inpatient visit. During the main visit, two nasoenteric tubes will be inserted through nostrils into the ileum (day 1) and duodenum (day 2). Tube placements will be performed by a consultant radiologist. The locations of tubes will be verified by fluoroscopy. Once tubes are in place, participants will receive one of the following intervention/control treatments on day 2 and day 3 in a randomised order; randomisation will be performed using the 'sealed envelope' website by an independent researcher (i.e., not linked to the study):

- Intervention arm: Participants will consume an oral drink through a straw within 5 minutes (T0–5 min). This is composed of maltose and glucose, which are simple sugars. Then Infusate D (a mixture of amino acids, the building bricks of proteins) will be infused to the duodenum from T30 to T120 minutes, and Infusate L (composed of simple sugars maltose, glucose and amino acids) to the ileum from 60 to 180 minutes. The drinks and infusates are composed of nutrients from food and are given in amounts that will reproduce the concentrations seen in the gut following food in our previous study.
- Control arm: Participants will consume an equal volume of a 0.9% saline solution as the drink. Then 0.9% saline solution will be infused into the duodenum and ileum at the corresponding rates and timeframes to match the intervention group.

Blood samples will be taken during the 0-180min period to measure appetite-related hormones, metabolite changes and glycaemic outcomes; Subjective appetite scores will be recorded; Urine samples will be collected to measure metabolite levels. After the infusion interventions, a pasta meal will be provided to measure food intake.

**Intervention Type**

Supplement

**Primary outcome measure**

Plasma concentrations of gut hormones including gastric inhibitory polypeptide (GIP), glucagon-like peptide-1 (GLP-1), peptide Y (PYY), cholecystokinin (CCK) and oxyntomodulin (OXM) are

measured by enzyme-linked immunosorbent assay (ELISA) or radioimmunoassay (RIA) assays at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes

### **Secondary outcome measures**

1. Appetite is measured using the visual analogue score (VAS) at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
2. Food intake is measured using an ad libitum pasta meal immediately after the 0-180 min intervention period
3. Plasma glucose concentrations are measured using the glucose oxidase-peroxidase aminophenazone phenol (GOD-PAP) method at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
4. Serum insulin concentrations are measured using an ELISA method at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
5. Blood metabolites are measured using proton nuclear magnetic resonance profiling (1H NMR profiling) at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
6. Urine metabolites are measured using 1H NMR profiling on post-infusion samples (collected over 0-180min)

### **Overall study start date**

01/01/2023

### **Completion date**

01/01/2028

## **Eligibility**

### **Key inclusion criteria**

1. Male or female
2. Age between 18-65 years (inclusive)
3. Body mass index (BMI) of 18-30 kg/m<sup>2</sup>
4. Willingness and ability to give written informed consent and willingness and ability to understand, to participate and to comply with the study requirements

### **Participant type(s)**

Healthy volunteer

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Upper age limit**

65 Years

### **Sex**

Both

### **Target number of participants**

Planned Sample Size: 15; UK Sample Size: 15

**Key exclusion criteria**

1. Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome
2. Abnormal ECG
3. Screening blood results outside of normal reference values
4. Weight change of  $\geq 5$  kg in the preceding 2 months
5. Current smokers
6. History of substance abuse and/or excess alcohol intake
7. Pregnancy
8. Diabetes
9. Cardiovascular disease
10. Cancer
11. Kidney disease
12. Liver disease
13. Pancreatitis
14. 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.
15. Participation in a research study in the 12-week period prior to entering this study.
16. Any blood donation within the 12-week period prior to entering this study
17. Previous surgery on the bones inside the nose, or nasal airway obstruction

Any participants with the above conditions would already have an altered pattern of hormones and inflammatory molecules because of their disease process and would therefore give us confounding or misleading results.

**Date of first enrolment**

01/04/2025

**Date of final enrolment**

01/04/2026

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre****NIHR Imperial Clinical Research Facility**

Imperial Centre for Translational and Experimental Medicine

Imperial College Healthcare NHS Trust

Hammersmith Hospital Campus

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# Sponsor information

## Organisation

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## Sponsor type

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## ROR

<https://ror.org/041kmwe10>

# Funder(s)

## Funder type

Research council

## Funder Name

Biotechnology and Biological Sciences Research Council

## Alternative Name(s)

UKRI - Biotechnology And Biological Sciences Research Council, BBSRC UK, BBSRC

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## Publication and dissemination plan

The study team will disseminate the results of the study via open-access, peer-reviewed scientific journal(s) within one year after the overall study end date. Work in progress will be presented at ISP group meetings and relevant conferences.

## Intention to publish date

01/01/2029

## Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version 4	29/01/2025	04/03/2025	No	Yes