

# Investigating the impact of glucagon timing and protein replacement on metabolism

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<b>Registration date</b> 01/02/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 28/05/2025	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<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 and fatty liver disease are very common problems in the UK affecting one in three people. These conditions are risk factors for type 2 diabetes. To treat diabetes, obesity and fatty liver disease, drug companies are developing drugs based on two hormones, glucagon-like peptide-1 and glucagon. Combined, these two hormones reduce weight, eliminate liver fat, and improve blood glucose control. Glucagon helps weight loss by increasing the amount of calories burnt, and also reduces fat (lipids) in the liver and the bloodstream.

However, treatment with the hormone glucagon may cause a reduction in circulating amino acids (the building blocks of protein and muscle). There is a possibility that a long-term reduction in circulating amino acids reduces muscle mass, which is extremely important for overall health. The aim of this study is to find out how to avoid low circulating amino acids by changing the timing of giving glucagon.

### Who can participate?

Males or females aged 18-65 years with a body mass index (BMI) between 25 and 45 kg/m<sup>2</sup> and with normal glucose control.

### What does the study involve?

Following an initial screening visit, participants will attend the Clinical Research Facility four times, and on each occasion will stay from Monday morning to Thursday afternoon (4 days, 3 nights). On each of the four visits to the Research Facility, participants will receive an infusion of either glucagon or placebo; This will occur through a cannula inserted into a vein in the arm. On one inpatient visit, the diet will also be supplemented with extra protein. The researchers will assess the effect of glucagon timing and dietary protein replacement on blood levels of amino acids and fat molecules. They will also monitor glucose control, appetite and energy expenditure.

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

Participants may not benefit directly from participating in the study. However, the information collected from this study will help us understand the best way of giving glucagon as a treatment for obesity and fatty liver disease. This may have a big impact in the future on the development

of drugs using glucagon. Expected side effects of a glucagon infusion include temporary nausea and vomiting, and possibly minor discomfort/bruising from insertion of the cannula into the arm for blood sampling and infusion.

Where is the study run from?

The study will be run from the NIHR/Wellcome Trust Imperial Clinical Research Facility (CRF) at the Hammersmith Hospital (UK). The study team is located at the Division of Metabolism, Digestion and Reproduction, Imperial College London at Hammersmith Hospital (UK).

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

September 2023 to July 2027

Who is funding the study?

Investigator initiated and funded

Who is the main contact?

Prof. Tricia Tan, [t.tan@imperial.ac.uk](mailto:t.tan@imperial.ac.uk).

## Contact information

### Type(s)

Public, Scientific, Principal Investigator

### Contact name

Prof Tricia Tan

### ORCID ID

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### Contact details

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## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

336170

### ClinicalTrials.gov number

Nil known

## Secondary identifying numbers

IRAS 336170

# Study information

## Scientific Title

The impact of glucagon timing and protein replacement on metabolism

## Acronym

GTPRO

## Study objectives

1. Continuous 24-h exposure to glucagon leads to amino acid breakdown
2. Excess amino acid breakdown may be avoided by timing glucagon in shorter 'bursts' during the day, mimicking the physiological variation of this hormone
3. Dietary protein supplementation also mitigates the reduction in circulating amino acids during a glucagon infusion

## Ethics approval required

Ethics approval required

## Ethics approval(s)

Approved 01/03/2024, London - Fulham Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; -; fulham.rec@hra.nhs.uk), ref: 24/LO/0044

## Study design

Single-blind randomized cross over study

## Primary study design

Interventional

## Secondary study design

Randomised cross over trial

## Study setting(s)

University/medical school/dental school

## Study type(s)

Efficacy

## Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet.

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

Overweight/obesity

## Interventions

Following an initial screening visit, participants will attend the NIHR Imperial Clinical Research Facility for a 4-day inpatient stay, where they will undergo a 72-hr intravenous infusion.

Participants will be allocated to the following groups in a cross-over design and receive intravenous infusions for 72 hours with a washout period:

Group 1. Continuous infusion of glucagon

Group 2. Continuous infusion of placebo

Group 3. Daytime infusion of glucagon (0800h to 2000h) and night-time infusion of saline (2000h to 0800h)

Group 4. Continuous infusion of glucagon with dietary protein supplementation

Participants allocated to receive glucagon (continuous or daytime) will receive increasing doses on study days 2 and 3, prior to discontinuation of the infusion on the morning of study day 4.

Doses of glucagon administered as an intravenous infusion will be as follows: Day 1 glucagon dose: 6 ng/kg/min, Day 2 glucagon dose: 12.5 ng/kg/min, Day 3 glucagon dose: 25 ng/kg/min,

Day 4: Infusion discontinued. Participants will be randomised to groups and a follow up visit will be arranged after completion of the four inpatient visits.

## **Intervention Type**

Drug

## **Pharmaceutical study type(s)**

Pharmacodynamic

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Glucagon

## **Primary outcome measure**

1. Circulating amino acids and lipids will be measured using mass spectrometry prior to infusion commencement, during the daytime and nighttime.

2. Energy expenditure will be measured using indirect calorimetry at baseline and at steady state during the infusion

## **Secondary outcome measures**

1. Appetite will be measured using visual analogue scales before and after each meal.

2. Glucose will be monitored using continuous glucose monitoring, over the 72 hour infusion period.

## **Overall study start date**

01/09/2023

## **Completion date**

01/07/2027

# **Eligibility**

## **Key inclusion criteria**

1. Aged 18-65 years

2. Male or female

3. Glycated haemoglobin (HbA1C) <48 mmol/mol

4. BMI 25-45 kg/m<sup>2</sup>, stable weight for >3 months

**Participant type(s)**

Healthy volunteer

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

65 Years

**Sex**

Both

**Target number of participants**

10

**Key exclusion criteria**

1. Diabetes mellitus of any type
2. Previous bariatric surgery
3. Current pregnancy or breastfeeding
4. History of having donated blood in the preceding 3 months
5. Alcohol intake >14 units/week
6. History of autoimmune liver disease or viral hepatitis
7. Pancreatic diseases
8. Severe gastrointestinal diseases
9. Drugs that affect hepatic steatosis
10. Subjects who have used prescription drugs within 4 weeks of first dosing, except antihypertensive treatments provided that the doses have not been altered within 4 weeks prior to entering the study
11. Subjects using Hypolipidaemic treatments
12. Subjects who have a history of relevant and severe atopy e.g. asthma, angioedema requiring emergency treatment, severe hayfever requiring regular treatment (i.e. taking antihistamines and/or glucocorticoids more regularly than 3 times a week), severe eczema requiring regular treatment (i.e. taking antihistamines and/or glucocorticoids more regularly than 3 times a week)
13. Subjects who have a history of relevant drug hypersensitivity
14. Subjects who have a history of alcohol abuse or alcohol dependence according to DSM-IV criteria within the last 2 years
15. Subjects who have a history of drug or substance abuse according to DSM-IV criteria within the last 2 years
16. Subjects who have a history of clinically significant migraine as judged by the Investigator. Subjects can be included if they have not had a migraine for the last 3 years
17. Subjects who have a significant infection or known inflammatory process on screening
18. Subjects who have acute gastrointestinal symptoms at the time of screening or admission (e.g. nausea, vomiting, diarrhoea, heartburn)
19. Subjects who have an acute infection such as influenza at the time of screening or admission
20. Subjects who have donated blood within 3 months prior to screening
21. Subjects who have donated plasma within the 7 days prior to screening
22. Subjects who have donated platelets within the 6 weeks prior to screening
23. Subjects who have used any investigational drug in any clinical trial within 3 months of their

first admission date

24. Subjects who have received the last dose of investigational drug greater than 3 months ago but who are on extended follow-up

**Date of first enrolment**

06/06/2024

**Date of final enrolment**

01/07/2026

## Locations

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**NIHR Imperial Clinical Research Facility**

Hammersmith Hospital

Du Cane Rd

Shepherd's Bush

London

United Kingdom

W12 0HS

## Sponsor information

**Organisation**

Imperial College London

**Sponsor details**

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Imperial College London and Imperial College Healthcare NHS Trust

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**Sponsor type**

University/education

**Website**

<http://www.imperial.ac.uk/>

**ROR**

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

## **Funder(s)**

**Funder type**

Other

**Funder Name**

Investigator initiated and funded

## **Results and Publications**

**Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal

**Intention to publish date**

01/08/2025

**Individual participant data (IPD) sharing plan**

All data generated or analysed during this study will be included in the subsequent results publication

**IPD sharing plan summary**

Published as a supplement to the results publication