

# How do hormones affect reproduction and metabolism in people with type 2 diabetes and people who do not have type 2 diabetes?

<b>Submission date</b> 29/11/2019	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 09/12/2019	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 26/02/2024	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Up to 40% of people who are obese and/or have type 2 diabetes have low reproductive hormone levels (hypogonadism) and therefore have reduced sexual function and reduced fertility. Also, having low reproductive hormone levels is associated with lower insulin secretion and higher insulin resistance in people with type 2 diabetes. Some hormones have been shown to be essential for fertility in animals and humans, whilst other hormones have been shown to affect the amount of insulin produced, appetite and body weight in animals and humans (but some of these effects might be different in different genders). Identifying hormones that can control both reproduction and metabolism may lead to better treatments for fertility disorders.

### Aims

Part A of the study will investigate if hormones, which are known to affect insulin and food intake and are produced in the gut (i.e. glucagon, glucagon-like peptide-1, oxyntomodulin, peptide-YY and substance P) can affect reproductive hormones.

Part B will investigate if certain reproductive hormones (i.e. kisspeptin and neurokinin B) can improve the ability of the body to respond to glucose how these hormones affect appetite, the quantity of food eaten and how much energy people use.

### Who can participate?

Men and women aged 18 – 60 years who are obese and/or have type 2 diabetes and are non-smokers.

### What does the study involve?

People will only be allowed to take part in both parts of the study at the same time.

In Part A, people who participate will come to the research facility for up to six visits. During one visit they will be given salty water through a plastic tube placed in a vein and during each of the other visits they will receive (through a plastic tube placed in a vein) a different hormone produced by the gut, which has been dissolved in salty water. The study visits will take place in a random order. During all study visits, blood samples will be taken (to measure hormone, glucose and insulin levels) through a plastic tube placed in a different vein.

In Part B, people who participate will come to the research facility for up to three pairs of visits. They will be asked to fast overnight before each study visit. For each pair of study visits, during one visit they will be given kisspeptin or neurokinin B (through a plastic tube placed in a vein) and salty water (through a plastic tube placed in a vein) on the other study visit. During one pair of study visits, they will be asked to drink a sugary drink. During the second pair of study visits, they will be given a sugar solution into a vein (via a plastic tube) with a small dose of insulin given to some people. During the third pair of study visits, they will be asked to rate their hunger levels, they will be given a meal to eat and in some cases measurements of how much energy they are using will be performed. During all study visits, blood samples will be taken (to measure hormone, glucose and insulin levels) through a plastic tube placed in a different vein.

What are the possible benefits and risks of participating?

**BENEFITS** - The information that we get from this study will help us to understand how to treat patients who suffer from type 2 diabetes, obesity and/or fertility problems.

**RISKS** - It is possible that mild nausea may occur. The insertion of the cannula may cause minor discomfort or superficial bruising. Some gut hormones can affect blood sugar but these effects do not last long. We will monitor blood sugar during the infusions and make sure that participants blood sugar is ok before they leave.

Where is the study run from?

Imperial College Academic Health Science Centre, UK

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

May 2019 to February 2023

Who is funding the study?

1. National Institute for Health Research, UK
2. Medical Research Council, UK
3. NIHR Imperial Biomedical Research Centre, UK
4. Society for Endocrinology, UK
5. Imperial College London, UK

Who is the main contact?

Dr Chioma Izzi-Engbeyaa  
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## Contact information

### Type(s)

Public

### Contact name

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**Type(s)**

Scientific

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## Additional identifiers

**Central Portfolio Management System (CPMS)**

20865

**Protocol serial number**

16HH3156

## Study information

**Scientific Title**

Physiological studies of hormones which control metabolism and reproduction

**Acronym**

REPROMET

**Study objectives**

The study aims to answer the questions:

Part A: Do gut hormones affect reproductive hormone secretion?

Part B: Do reproductive hormones affect gut hormones, glucose, insulin, appetite, food intake and energy expenditure?

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Approved 26/04/2016, West London & GTAC Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)207 104 8124; NRESCommittee.London-WestLondon@nhs.net), ref: 16/LO/0391

## **Study design**

Single-blinded randomized two-way crossover study

## **Primary study design**

Interventional

## **Study type(s)**

Other

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

Reproductive hormone effects

## **Interventions**

Part A: Intravenous infusion of vehicle during one study visit and intravenous infusion of a gut hormone (i.e. glucagon, glucagon-like peptide-1, oxyntomodulin, peptide-YY or substance P) during a separate study visit. Infusion order will be randomly assigned

Part B (participants will be involved in one or more of the following):

1: Intravenous infusion of vehicle during one study visit and intravenous infusion of a reproductive hormone (kisspeptin or neurokinin B) during a separate study visit. Infusion order will be randomly assigned. Oral glucose tolerance tests (OGTT) will be performed during both study visits

2: Intravenous infusion of vehicle during one study visit and intravenous infusion of a reproductive hormone (kisspeptin or neurokinin B) during a separate study visit. Infusion order will be randomly assigned. Intravenous glucose tolerance tests (IVGTT) will be performed during both study visits

3: Intravenous infusion of vehicle during one study visit and intravenous infusion of a reproductive hormone (kisspeptin or neurokinin B) during a separate study visit. Infusion order will be randomly assigned. Mixed meal tolerance tests (MMTT) will be performed during both study visits

Randomisation:

Part A – An online random number generator ([www.random.org](http://www.random.org)) will be used to generate numbers for each participant at the time of study entry. Participants with an even number will receive vehicle infusion first and glucagon-like peptide-1 (GLP-1) infusion second. Participants with an odd number will receive GLP-1 infusion first and vehicle infusion second. This process will be repeated for paired peptide-YY infusion and vehicle infusion visits; glucagon infusion and vehicle infusion visits; oxyntomodulin infusion and vehicle infusion visits; and substance P infusion and vehicle infusion visits.

Part B – An online random number generator ([www.random.org](http://www.random.org)) will be used to generate numbers for each participant at the time of study entry. Participants with an odd number will

receive kisspeptin infusion first and vehicle infusion second. Participants with an even number will receive vehicle infusion first and kisspeptin infusion second. This process will be repeated for paired neurokinin B infusion and vehicle infusion visits

## **Intervention Type**

Other

## **Primary outcome(s)**

Part A:

1. Luteinising hormone (LH) pulsatility, LH levels, follicle-stimulating hormone levels and testosterone levels in males measured using blood tests during the vehicle and hormone infusions
2. Oestrogen and progesterone levels in females measured blood tests during the vehicle and hormone infusions

Part B:

1. OGTT/IVGTT/MMTT insulin and glucose levels measured using blood tests during vehicle and hormone infusions
2. OGTT/IVGTT/MMTT insulin secretion measured using blood tests during vehicle and hormone infusions
3. OGTT/IVGTT/MMTT insulin sensitivity and disposition indices measured using blood tests during vehicle and hormone infusions
4. MMTT food intake measured using scales during vehicle and hormone infusions
5. MMTT Energy expenditure measured using calorimetry and infrared thermography during vehicle and hormone infusions

## **Key secondary outcome(s)**

Part B: Pre- and post-meal nausea, hunger and fullness ratings measured using visual analogue scales during hormone and vehicle infusions.

## **Completion date**

01/02/2023

## **Eligibility**

### **Key inclusion criteria**

1. Aged 18 – 60 years
2. Male or female
3. Stable body weight for the preceding 3 months
4. 12-lead ECG with no clinically significant abnormalities as judged by the investigators
5. Full blood count, urea and electrolytes, thyroid function tests, liver function tests and glucose within 2 x the upper limit of normal
6. Conditions that predispose subfertility: BMI >25, Pre-diabetes, Type 2 diabetes

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

Mixed

### **Healthy volunteers allowed**

No

### **Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

60 years

**Sex**

All

**Total final enrolment**

78

**Key exclusion criteria**

1. History of any medical, psychological or other condition, or use of any medications, including over-the-counter products, which, in the opinion of the investigators, would either interfere with the study or potentially cause harm to the volunteer
2. Pregnancy or breastfeeding
3. History of hypersensitivity to any of the components of the infusions
4. Treatment with an investigational drug within the preceding 2 months
5. Volunteers who have or intend to donate blood or blood products within three months before or following study completion
6. A history of alcoholism or substance abuse within the preceding 5 years
7. A history of major haematological, renal, thyroid or hepatic abnormalities or significant cardiovascular disease
8. A history of cancer
9. Volunteers with a medical or psychological condition that would impair their ability to participate reliably in the study or give informed consent
10. Smoker

**Date of first enrolment**

23/05/2019

**Date of final enrolment**

01/02/2023

**Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Imperial College Academic Health Science Centre**  
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W6 8RF

## Sponsor information

### Organisation

Imperial College London

## Funder(s)

### Funder type

Government

### Funder Name

National Institute for Health Research

### Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

### Funder Name

Medical Research Council

### Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

**Location**

United Kingdom

**Funder Name**

NIHR Imperial Biomedical Research Centre

**Alternative Name(s)**

NIHR Imperial BRC, Imperial Biomedical Research Centre, BRC

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Research institutes and centers

**Location**

United Kingdom

**Funder Name**

Society for Endocrinology

**Alternative Name(s)**

The Society for Endocrinology, SFE

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

**Funder Name**

Imperial College London

**Alternative Name(s)**

Imperial College of Science, Technology and Medicine, Imperial College London, UK, Imperial College London, London, England, Imperial College London in United Kingdom, imperialcollege, ICL

**Funding Body Type**

Government organisation

## Funding Body Subtype

Universities (academic only)

## Location

United Kingdom

## Funder Name

NIHR Academy; Grant Codes: RP-2014-05-001

# Results and Publications

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available as this study is a physiological study.

## IPD sharing plan summary

Not expected to be made available

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	Effects of Peptide YY on the reproductive axis in healthy young men	01/03/2020	03/12/2019	Yes	No
<a href="#">Results article</a>	Effects of kisspeptin on glucose-stimulated insulin secretion, metabolites, gut hormones, appetite and food intake in healthy men	01/12/2018	03/12/2019	Yes	No
<a href="#">Results article</a>	Effects of kisspeptin on food intake in women with overweight or obesity	11/04/2023	17/04/2023	Yes	No
<a href="#">Results article</a>	Acute effects of glucagon on reproductive hormone secretion in healthy men	01/06/2020	26/02/2024	Yes	No
<a href="#">Results article</a>	Effects of glucagon-like peptide-1 on the reproductive axis in healthy men	01/04/2020	26/02/2024	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version V2	18/03/2019	09/12/2019	No	No