

# Improving hormonal infertility treatment for men with hypogonadotropic hypogonadism

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| <b>Submission date</b><br>30/01/2025   | <b>Recruitment status</b><br>Recruiting                        | <input type="checkbox"/> Prospectively registered               |
|  |  | <input type="checkbox"/> Protocol                               |
| <b>Registration date</b><br>30/04/2025 | <b>Overall study status</b><br>Ongoing                         | <input type="checkbox"/> Statistical analysis plan              |
|  |  | <input type="checkbox"/> Results                                |
| <b>Last Edited</b><br>09/02/2026       | <b>Condition category</b><br>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

Hypogonadotropic hypogonadism (HH) affects 1 in 2000 men and is the only type of male infertility which can be reversed with medications. Men with HH have little or no sperm in the semen because their brains do not make the hormones (gonadotrophins) needed to 'switch on' their testes. Gonadotrophin injections are used in the NHS to restore sperm for some men with HH, helping their partners get pregnant. However, gonadotrophin injections sometimes do not work at all, or give too few sperm for pregnancy without female fertility treatments (like in vitro fertilisation [IVF]). Furthermore, three different 'gonadotrophin recipes' are commonly used in the NHS. Doctors do not know which gonadotrophin recipe is best for pregnancy since no study has been large enough to answer this. Gonadotrophins are very expensive. Working out which recipe gives the best chance of pregnancy would be a major improvement in the quality of fertility treatment. Many other factors (e.g. age of female partner) are also likely to affect pregnancy outcomes, but lack of evidence limits the advice we can give couples with HH about the chance of a successful pregnancy.

This study aims to find out:

1. Which recipe of gonadotrophin treatment in men with HH has the highest chance of pregnancy?
2. Which other factors are associated with pregnancy during gonadotrophin treatment?
3. What factors are associated with needing either female fertility treatment or side effects during gonadotrophin treatment?

### Who can participate?

Adult men diagnosed with HH, either congenital or acquired

### What does the study involve?

We are not recruiting any patients for this study. We will look back at what happened to men with hypogonadotropic hypogonadism who have already completed gonadotrophin treatment in specialist hospitals around the world. We will ask specialists around the world to examine their medical records and to send us the results of their treatment between 1995 and 2023 to analyse. By studying their results and details about the patients we will try to answer the above questions.

What are the possible benefits and risks of participating?

Data is collected from medical records of patients who have already been treated with this treatment. There are no risks to participating. There are no direct benefits, however, this information will help inform future care of men with infertility from hypogonadotropic hypogonadism.

Where is the study run from?

Imperial College Healthcare NHS Trust (UK)

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

October 2023 to January 2028

Who is funding the study?

National Institute for Health and Care Research – Research for Patient Benefit Grant (UK)

Who is the main contact?

Dr Bonnie Grant, b.grant@imperial.ac.uk

## Contact information

### Type(s)

Public

### Contact name

Dr Bonnie Grant

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### Type(s)

Principal investigator

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

347624

### ClinicalTrials.gov (NCT)

Nil known

### National Institute for Health and Care Research (NIHR)

207215

### Central Portfolio Management System (CPMS)

64996

## Study information

### Scientific Title

Improving hormonal treatment for men with infertility due to hypogonadotropic hypogonadism (HHF study)

### Acronym

HHF

### Study objectives

Fertility treatment using gonadotropin therapy in men with hypogonadotropic hypogonadism (HH) will improve sperm production and overall fertility outcomes, with variations in success rates depending on multiple factors such as patient age, testosterone levels, treatment regime and partner characteristics.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approved 17/10/2024, Health Research Authority (2 Redman Place, Stratford, London, E20 1JQ, UK; Tel: not available; HCRW. approvals@wales.nhs.uk), ref: 24/HRA/4318

## **Study design**

Observational; Design type: Cross-sectional

## **Primary study design**

Observational

## **Study type(s)**

Treatment

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

Infertility due to hypogonadism

## **Interventions**

Retrospective study of anonymised data from case notes (obtaining treatment details from patient records without any identifiable information)

The researchers will not recruit any participants for this study. Collaborating hospitals will review their records to identify men with hypogonadotropic hypogonadism (HH) whom they treated for fertility between 1995 to 2023. They will collect clinical details of patients without any identifiable information. The teams will share data with the Imperial College London and the University of Aberdeen. Statisticians from the University of Aberdeen will analyse data from all centres to answer the research questions. They will perform some complex analyses to identify which 'treatment recipe' works best and which patient and partner factors will suggest a good response to treatment.

## **Intervention Type**

Other

## **Primary outcome(s)**

Reported pregnancy in partner of patient collected from patient records at single timepoint of reported pregnancy

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

1. Time to pregnancy in partner of patient, collected from patient records, at single timepoint of reported pregnancy
2. Use of assisted reproductive technology, collected from patient records, at single timepoint of reported use of ART
3. Appearance of sperm in the semen (in men with baseline azoospermia or inability to produce semen), collected from patient records, at multiple timepoints when semen sample performed (will vary between patients)
4. Sperm concentration >5 million/ml (in men with azoospermia/ inability to produce semen or sperm concentration <5 million/mL), collected from patient records, at multiple timepoints when semen sample performed (will vary between patients)
5. Live birth rates in the partner, collected from patient records at single timepoint of reported live birth
6. Reported adverse effects, collected from patient records at multiple timepoints when adverse effect reported

## **Completion date**

01/01/2028

# Eligibility

## Key inclusion criteria

1. Adult men diagnosed with HH based on the clinical features of hypogonadism, low testosterone, and low gonadotropins
2. Pre-treatment sperm concentration <5 million/mL – congenital and acquired cases will be included
3. Treatment with gonadotrophins between 1995 to 2023
4. Follow-up for at least 2 years or until pregnancy in the partner, whichever is sooner

## Participant type(s)

Patient

## Healthy volunteers allowed

No

## Age group

Mixed

## Lower age limit

18 years

## Upper age limit

100 years

## Sex

Male

## Total final enrolment

0

## Key exclusion criteria

1. Concomitant primary hypogonadism
2. Suspicion of reversible aetiology for HH e.g., anabolic steroids, opioids, morbid obesity

## Date of first enrolment

01/03/2025

## Date of final enrolment

31/08/2026

# Locations

## Countries of recruitment

United Kingdom

England

France

Germany

Italy

Türkiye

United States of America

**Study participating centre**

**Imperial College Healthcare NHS Trust**

The Bays

St Marys Hospital

South Wharf Road

London

England

W2 1BL

**Study participating centre**

**The Newcastle upon Tyne Hospitals NHS Foundation Trust**

Freeman Hospital

Freeman Road

High Heaton

Newcastle upon Tyne

England

NE7 7DN

**Study participating centre**

**University College London Hospitals NHS Foundation Trust Hq**

235 Euston Road

London

England

NW1 2BU

**Study participating centre**

**Lothian NHS Board**

Waverleygate

2-4 Waterloo Place

Edinburgh

Scotland

EH1 3EG

**Study participating centre**

**University Hospitals Birmingham NHS Foundation Trust**  
Queen Elizabeth Hospital Birmingham  
Mindelsohn Way  
Edgbaston  
Birmingham  
England  
B15 2GW

**Study participating centre**  
**Unit for Gynecological and Andrological Endocrinology**  
Dept. of Medical Biotechnology and Translational Medicine  
University of Milan  
Via Festa del Perdono, 7  
Milano  
Italy  
20122

**Study participating centre**  
**University of Modena and Reggio Emilia**  
Via Università, 4  
Modena  
Italy  
41121

**Study participating centre**  
**Istanbul University**  
Beyazıt  
Fatih/İstanbul  
Türkiye  
34452

**Study participating centre**  
**Clinical Andrology**  
Centre for Reproductive Medicine and Andrology  
Domagkstrasse 11  
Münster  
Germany  
D-48149

**Study participating centre**

**Harvard University**  
Massachusetts Hall  
Cambridge  
United States of America  
02138

**Study participating centre**  
**Université Paris Saclay**  
3 rue Joliot Curie  
Bâtiment Breguet  
Gif-sur-Yvette  
France  
91190

**Study participating centre**  
**Concord Repatriation General Hospital**  
Andrology Department  
Sydney Local Health District  
Sydney  
Australia  
2137

## **Sponsor information**

**Organisation**  
Imperial College London

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

## **Funder(s)**

**Funder type**  
Government

**Funder Name**  
National Institute for Health and Care 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

## **Results and Publications**

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

**IPD sharing plan summary**

Not expected to be made available