

Improving hormonal infertility treatment for men with hypogonadotropic hypogonadism

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

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

347624

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

CPMS 64996, NIHR207215

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

Secondary study design

Cross sectional study

Study setting(s)

Hospital

Study type(s)

Treatment

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

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

Phase

Not Specified

Primary outcome measure

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

Secondary outcome measures

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

Overall study start date

10/10/2023

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

Age group

Adult

Lower age limit

18 Years

Sex

Male

Target number of participants

Planned Sample Size: 300; UK Sample Size: 300

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

28/02/2026

Locations

Countries of recruitment

England

France

Germany

Italy

Türkiye

United Kingdom

United States of America

Study participating centre

Imperial College Healthcare NHS Trust

The Bays

St Marys Hospital

South Wharf Road

London

United Kingdom

W2 1BL

Study participating centre

The Newcastle upon Tyne Hospitals NHS Foundation Trust

Freeman Hospital

Freeman Road

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University College London Hospitals NHS Foundation Trust Hq

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Study participating centre

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Study participating centre

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Mindelsohn Way
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United Kingdom
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Study participating centre

Unit for Gynecological and Andrological Endocrinology

Dept. of Medical Biotechnology and Translational Medicine
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Study participating centre

University of Modena and Reggio Emilia

Via Università, 4
Modena
Italy
41121

Study participating centre

Istanbul University

Beyazıt
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Türkiye
34452

Study participating centre

Clinical Andrology

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Study participating centre
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Study participating centre
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Sponsor type
University/education

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ROR
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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

Publication and dissemination plan

We plan to publish in a high-impact peer-reviewed journal around 1 year after the study end date. We also plan to present findings at international conferences. We will develop online patient resources including a lay English summary and infographics of our findings with the help of our PPI lead hosted by Imperial College. These will be shared on the patient support groups including the 'Kallman Syndrome' Facebook group, 'I am HH' patient support group and the 'Pituitary Foundation'. We will also approach the 'hypogonadism support group' of the Drugs.com website to post the results as news on their website. We will present our results to the Patients attending ENDO conference and BES conference as well. Media coverage at those two conferences will also help to disseminate the results to the wider public.

Intention to publish date

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to being outside terms of ethical agreement on data sharing.

IPD sharing plan summary

Not expected to be made available