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Improving hormonal infertility treatment for men with hypogonadotropic hypogonadism

Submission date
30/01/2025

Recruitment status
Recruiting

Registration date
30/04/2025

Overall study status
Ongoing

Last Edited
30/04/2025

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] 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

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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
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Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
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Study participating centre
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Sponsor type
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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