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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
09/02/2026

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?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
347624

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
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W2 1BL

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
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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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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
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Study participating centre
Istanbul University
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34452

Study participating centre
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Study participating centre

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Study participating centre
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Study participating centre
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Andrology Department
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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