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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

Type(s)
Public

Contact name
Dr Bonnie Grant

ORCID ID
https://orcid.org/0000-0003-1121-9211

Contact details
6th Floor, Commonwealth Building
Imperial College London
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0NN
+44 (0)20 7594 2489
b.grant@imperial.ac.uk

Type(s)
Principal investigator

Contact name
Dr Channa Jayasena

ORCID ID
https://orcid.org/0000-0002-2578-8223

Contact details

6th Floor, Commonwealth Building
Imperial College London
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0NN
+44 (0)20 7594 2489
c.jayasena@imperial.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
347624

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

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

Phase
Not Specified

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
Adult

Lower age limit
18 years

Sex
Male

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
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
United Kingdom
W2 1BL

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
University College London Hospitals NHS Foundation Trust Hq
235 Euston Road
London
United Kingdom
NW1 2BU

Study participating centre
Lothian NHS Board
Waverleygate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham

United Kingdom
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

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes