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A clinical trial of clomifene citrate in men with infertility

Submission date	Recruitment status	[X] Prospectively registered
28/02/2026	Recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/07/2026	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
14/07/2026	Urological and Genital Diseases	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Male infertility affects many couples trying to conceive. In some men, infertility may be linked to low testosterone levels caused by problems with hormone signals that control the testes (secondary functional hypogonadism), while in others, the cause is unknown (idiopathic male infertility).

Clomifene citrate is a medication that is commonly used to treat female infertility and may help improve sperm production in men. However, more research is needed to determine how effective and safe it is for treating male infertility.

This study aims to investigate whether clomifene citrate can improve sperm concentration and fertility outcomes in men with secondary functional hypogonadism or idiopathic male infertility compared with a placebo.

Who can participate?

Men aged 18 to 44 years who have been trying to conceive for at least 12 months and have abnormal semen parameters or secondary functional hypogonadism.

What does the study involve?

A total of 160 men will take part across several NHS hospitals in the UK.

Participants will be randomly allocated to receive either:
- One 25 mg clomifene citrate tablet daily
- A placebo tablet daily

Neither participants nor the study team will know which treatment has been allocated.

Participants will take the study medication for 9 months.

They will attend follow-up visits at 3, 6, and 9 months, where they will:

Provide semen samples for analysis
Have blood tests
Have health assessments
Complete questionnaires about quality of life and sexual health

Researchers will also collect information about pregnancies and fertility treatments. A final follow-up assessment will take place 18 months after joining the study.

What are the possible benefits and risks of participating?
Participants may benefit if clomifene citrate improves sperm production and fertility outcomes. The information collected may help improve future treatment options for men with infertility.

Clomifene has a well-established safety profile but may cause mild to moderate side effects. There is also a possibility of interactions with some medications. Participants will be closely monitored throughout the study, including regular blood tests and safety reviews.

Where is the study run from?
University College London (UCL) Comprehensive Clinical Trials Unit, UK.

When is the study starting and how long is it expected to run for?
August 2026 to February 2029.

Who is funding the study?
National Institute for Health and Care Research (NIHR), UK.

Who is the main contact?
Rumana Jalil, cctu.concrete@ucl.ac.uk

Contact information

Type(s)
Scientific, Public

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Integrated Research Application System (IRAS)
1012496

Central Portfolio Management System (CPMS)
69132

National Institute for Health and Care Research (NIHR)
167189

Sponsor's protocol code number
CTU/2023/46

Study information

Scientific Title
Effectiveness of ClOmifeNe CitRate for the management of mEn wiTh infErtility (CONCRETE): A randomised double-blind placebo-controlled trial.

Acronym
CONCRETE

Study objectives
The primary aim of CONCRETE is to evaluate the efficacy and safety of clomifene as a treatment for men with secondary hypogonadism or idiopathic male infertility compared to placebo.

Secondary objective:
1. To determine the efficacy of clomifene in improving semen parameters in this group of men.
2. To determine the efficacy of clomifene in improving the reproductive outcomes in this group of men.
3. To determine the safety of clomifene as a treatment for men with secondary hypogonadism or idiopathic male infertility.
4. To explore the feasibility and acceptability of using clomifene as a primary treatment in this group of men.

Ethics approval required
Ethics approval required

Ethics approval(s)

Submitted 27/02/2026, Yorkshire & The Humber - Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; -; leedswest.rec@hra.nhs.uk), ref: 26/YH/0057

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Single

Purpose
Treatment, Safety

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Male infertility

Interventions
Patients will be randomised using the Sealed envelope platform on the computer to receive either 25mg Clomifene Citrate or a matching placebo, to be taken orally once a day for 9 months.
• Experimental Arm: 25mg Clomifene Citrate
• Control Arm: Placebo

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Clomifene citrate

Primary outcome(s)
1. Sperm concentration measured using semen analysis (millions per millilitre (millions/mL) at the 6-month visit

Key secondary outcome(s)
1. Sperm concentration measured using semen analysis at 3-, and 9-month visits

2. Total sperm count as per WHO criteria measured using semen analysis at 3-, 6- and 9-month visits

3. Percent of total sperm motility as per WHO criteria measured using semen analysis at 3-, 6- and 9-month visits

4. Percent of progressive sperm motility as per WHO criteria measured using semen analysis at 3-, 6- and 9-month visits

5. Percent of normal sperm morphology as per WHO criteria measured using semen analysis at 3-, 6- and 9-month visits

6. Incidence of spontaneous clinical pregnancy measured using data collection from patient records at the 18-month visit

7. Incidence of the need to use any Assisted Reproductive Technology (ART) treatments measured using data collection from patient records at the 18-month visit

8. Incidence of pregnancy outcome (spontaneous or with ART) including miscarriage, stillbirth, livebirth and neonatal death measured using data collection from patient records at the 18-month visit

9. Time to the first incidence of pregnancy from randomisation measured using data collection from patient records at the 18-month visit

10. Incidence of the need to undergo Surgical Sperm Retrieval (SSR) procedure, the type and the outcome of the SSR procedure measured using data collection from patient records at the 18-month visit

11. Biochemical outcomes: LH, FSH, Oestradiol, early rise total and free testosterone, oestradiol: testosterone ratio, sex hormone-binding globulin, prolactin, kidney and liver function profile measured using standard medical laboratory methods at the 3-, 6- and 9-month visits

12. Clinical outcome: BMI (kg/m2) measured using standard methods at the 3-, 6- and 9-month visits

13. Quality of Life outcomes measured using the Male Sexual Health Questionnaire (MSHQ) and the EQ-5D-5L questionnaire at the 3-, 6-, 9- and 18-month visits

14. Adverse Events and Reactions (AEs/ARs) at all grades and Serious Adverse Events and Reactions (SAEs/SARs) at all grades measured using data from Case Report Forms (CRFs) at any time throughout the duration of the trial

Completion date
28/02/2029

Eligibility

Key inclusion criteria
1. Men assigned as biological male at birth
2. Aged ≥18-<45 years inclusive at baseline and randomisation.

3. Diagnosis of primary or secondary infertility at the time of screening, having been trying to conceive for ≥12 months with abnormal semen parameters due to:
(i) reduced sperm concentration of ≤16 million spermatozoa per ml on as per the WHO criteria, or
(ii) secondary functional hypogonadism (defined as early rise total testosterone ≤12pmol/l) after excluding other causes
4. Capacity to give informed consent

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Male

Total final enrolment
0

Key exclusion criteria
1. Primary testicular failure (confirmed with an FSH level of ≥15 IU/L) at time of screening
2. History of primary or secondary hypogonadotropic hypogonadism due to other congenital or acquired condition disturbing the hypothalamic-pituitary gonadal axis.
3. History of taking prescribed or non-prescribed hormonal treatment therapy including but not limited to clomifene, gonadotrophins, anabolic steroids and exogenous testosterone.
4. Other causes of male infertility including but not limited to; known obstructive azoospermia, untreated clinical varicocele, history of mumps orchitis, history of chemotherapy/radiotherapy treatment.
5. Abnormal karyotype, evidence of Y chromosome AZF microdeletion, cystic fibrosis gene abnormality, history of cryptorchidism

Date of first enrolment
01/08/2026

Date of final enrolment
31/07/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College London Hospital
250 Euston Road
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Study participating centre
Epsom and St Helier University Hospitals NHS Trust
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Study participating centre
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Queen Victoria Road
Newcastle upon Tyne
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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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M13 9WL

Study participating centre
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Guy's Hospital, Great Maze Pond
London
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SE1 9RT

Sponsor information

Organisation
University College London Comprehensive Clinical Trials Unit

Funder(s)

Funder type

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

Data will be shared based on the following principles:
o No data should be released that would compromise an ongoing trial or study.
o There must be a strong scientific or other legitimate rationale for the data to be used for the requested purpose.
o Investigators who have invested time and effort into developing a trial or study should have a period of exclusivity in which to pursue their aims with the data before key trial data are made available to other researchers.
o The funder's requirements for data sharing will be adhered to.
o The resources required to process requests should not be underestimated, particularly successful requests which lead to preparing data for release. Therefore, adequate resources must be available to comply in a timely manner or at all, and the scientific aims of the study must justify the use of such resources.
o Data exchange complies with Information Governance and Data Security Policies in all of the relevant countries.
o Data will be available for sharing after publication of the primary trial results. Researchers wishing to access CONCRETE trial data should contact the Trial Management Group, cctu.concrete@ucl.ac.uk, in the first instance.

IPD sharing plan summary

Available on request