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ESTEEM: A clinical trial testing whether testosterone can help improve the quality of life during menopause

Submission date
27/09/2025

Recruitment status
Not yet recruiting

Registration date
22/12/2025

Overall study status
Ongoing

Last Edited
08/05/2026

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The ESTEEM trial is testing whether adding testosterone to standard Hormone Replacement Therapy (HRT) can help improve menopause-related quality of life. Many women still have symptoms such as poor sleep, brain fog, headaches, hot flushes, low mood and low energy even when taking HRT. Testosterone is already used to improve sexual function in post-menopausal women, but its effects on these wider symptoms are not well understood. This trial will also look at any possible side effects, such as acne or hair growth, to weigh up the benefits and risks.

Around 13 million women in the UK are peri- or post-menopausal, and up to a quarter experience severe symptoms that can last for several years. HRT is the most effective treatment, but it does not always fully relieve symptoms. By testing whether testosterone can help with a broader range of symptoms, the trial aims to generate evidence to guide future NHS care.

Who can participate?
The trial is open to peri- and post-menopausal women in the UK who are already on standard doses of HRT for at least 6 months but still have symptoms. Women cannot take part if they have recently used testosterone or certain other hormone medicines.

What does the study involve?
Participants will be randomly allocated to use either testosterone cream or a placebo cream, in addition to their usual HRT, for 12 months. Neither participants nor their doctors will know which treatment they are receiving. They will be asked to complete online questionnaires about their symptoms and quality of life at the start, and again at 3, 6 and 12 months. Blood tests will be taken at the same time points to monitor safety. Some participants and healthcare professionals will also be interviewed to share their views and experiences. The study will run across the UK, with women able to join remotely or through GP practices. Each woman will take part for 12 months.

What are the possible benefits and risks of participating?
By taking part, women will help researchers find out whether testosterone can improve

menopause symptoms that are not well managed by HRT, such as sleep problems, brain fog, or lack of energy. This evidence could improve future NHS care for women experiencing the menopause. Some women may also notice an improvement in their own symptoms, although this cannot be guaranteed.

Like all medicines, testosterone cream can have side effects. These may include acne, oily skin, or increased hair growth, and in rare cases, more serious issues. The study includes regular safety monitoring and medical follow-up. Participation also involves a time commitment for blood tests, daily treatment, and completion of questionnaires.

Where is the study run from?
Cardiff University, UK

When is the study starting and how long is it expected to run for?
September 2025 to October 2028

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

Who is the main contact?
esteem@cardiff.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

Integrated Research Application System (IRAS)
1008601

Central Portfolio Management System (CPMS)
58305

Protocol serial number
SPON 2006-24

Study information

Scientific Title
ESTEEM: Evaluating the clinical and cost-effectiveness of testosterone to improve menopause-related quality of life

Acronym
ESTEEM

Study objectives
To establish the effectiveness of testosterone in reducing menopausal symptoms, beyond altered sexual function, in women already receiving standard HRT as measured by a validated tool of menopause-specific quality of life

1. Confirm feasibility of adequate and equitable trial recruitment, retention and data quality in an internal pilot
2. Establish the cost-effectiveness of testosterone based on a primary outcome of Quality Adjusted Life Years
3. Assess safety profile and potential harms of testosterone treatment
4. Gain patient consent and link data to allow long-term monitoring of health outcomes using routinely collected data
5. Explore barriers/facilitators amongst service providers and women to future prescribing and

uptake of testosterone
6. Work with lay research partners to design, deliver and report a trial that meets the needs of all women who may experience menopausal symptoms

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/01/2026, London - Fulham Research Ethics Committee (Skipton House, 80 London Road, London, SE1 6LH, United Kingdom; +44 20 7104 8000; fulham.rec@hra.nhs.uk), ref: 25/LO/0770

Study design
Randomized placebo-controlled double-blind parallel-group study

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Medical condition: Menopause
Medical condition in lay language: Menopause
Therapeutic areas: Diseases [C] - Female diseases of the urinary and reproductive systems and pregancy complications [C13]

Interventions
• Arm 1 (Intervention): AndroFeme® 1% testosterone cream, transdermal route. The intervention dose uses two pumps (each delivering 0.5 g of 1% testosterone gel, equivalent to 5 mg testosterone per day), applied once daily to the lower abdomen or upper thigh for 12 months in addition to standard HRT.
• Arm 2 (Placebo): Matching placebo cream, 2 pumps daily, transdermal route, for 12 months in addition to standard HRT.
• Follow-up: Baseline, 3, 6 and 12 months with questionnaires, blood sampling, and app-based safety and treatment adherence monitoring.
• Randomisation: Centralised online randomisation system, 1:1 allocation using concealed allocation.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
AndroFeme® 1% testosterone cream [Testosterone]

Primary outcome(s)

Menopause-related quality of life measured using the Menopause-Specific Quality of Life-Intervention (MENQOL-I) questionnaire. Summary scores will be assessed over time, incorporating 3-, 6- and 12-month responses

Key secondary outcome(s))
The following secondary outcome measures are assessed at baseline, 3, 6 and 12 months, unless stated:
1. Menopause-related quality of life measured using the MENQOL-I questionnaire (individual domains: vasomotor, psychosocial, physical functioning, sexual; plus total summary score)
2. Sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI)
3. Everyday memory performance measured using the Everyday Memory Questionnaire – Revised (EMQ-R)
4. Depressive symptoms measured using the Patient Health Questionnaire (PHQ-9)
5. Anxiety symptoms measured using the Generalised Anxiety Disorder Assessment (GAD-7)
6. Migraine-related quality of life measured using the Migraine-Specific Quality of Life Questionnaire (MSQoL)
7. Satisfaction with treatment measured using the Menopause Symptoms Treatment Satisfaction Questionnaire (MS-TSQ)
8. Health-related quality of life measured using the EQ-5D-5L instrument
9. Capability and wellbeing measured using the ICECAP-A instrument
10. Healthcare resource use measured using a trial-specific resource-use questionnaire
11. Body measurements: participants will provide their height and weight (to calculate BMI) and measure waist circumference at home using a simple tape-measure method
12. Adverse events self-reported via the mobile phone Trial App throughout the trial and summarised at 12 months
13. Adherence to treatment measured using participant weekly self-reporting via the mobile phone Trial App and assessed monthly

Completion date
30/10/2028

Eligibility

Key inclusion criteria
1. Women receiving standard HRT for at least 6 months who remain symptomatic
2. Willing to stay on current standard HRT for duration of trial
3. Able/willing to provide informed consent, including proof of ID
4. At any stage in perimenopause or menopause, including those with Premature Ovarian Insufficiency and medical/surgical menopause already taking standard HRT
5. Able to receive transdermal testosterone
6. Able/willing to adhere to a 12-month follow-up (including regular use of app throughout the trial participation)
7. Able/willing to have blood tests at baseline, 3, 6 and 12 months and as necessary
8. Individuals assigned female sex at birth who are aged > 45 years at the time of consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Women with altered sexual function as their only symptom attributed to the menopause.
2. High baseline testosterone level outside the pre-menopausal physiological range (above 2.6 nmol/l by immunoassay)
3. Allergy to almonds
4. Pregnant, breastfeeding, planning to become pregnant during the study period, or of childbearing potential and not using a protocol-approved method of contraception.
5. Active malignancy or treatment for malignancy (<6/12); known or suspected carcinoma of the breast; known or suspected androgen-dependent neoplasia
6. Women with nephrotic syndrome
7. History of hypercalcaemia
8. Involvement in another clinical trial for investigational medicinal product (CTIMP) at the time of consent
9. Androgen treatment (testosterone or tibolone) or antiandrogen therapy within the past 6 months (eg. Spironolactone, finasteride, minoxidil, cyproterone)
10. Women who are also using; oral anticoagulants, corticosteroids or adrenocorticotropic hormone (ACTH), oxyphenbutazone, bupropion, ciclosporin, conjugated equine estrogens and any oral contraception containing an estrogenic steroid hormone
11. Less than 1 month use of complementary and/or prescribable non-hormonal alternatives to HRT, which have been shown in trial to be of benefit, such as Fezolinetant, Oxybutinin, Selective Serotonin Reuptake Inhibitor (SSRI), or SNRI/SSRI, Gabapentin, Pregabalin, Clonidine, St Johns Wort, Isoflavones and Black Cohosh.

Date of first enrolment
01/06/2026

Date of final enrolment
30/11/2027

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre

Cardiff University
(non-NHS participating site, potential participants can self-refer directly to the central trial team via the trial website, NHS recruitment via primary care hubs and general practices (GPs) across England and Wales (full site list to be added once contracts are in place)
Cardiff
Wales
CF10 3AT

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

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 the ESTEEM trial will be available on reasonable request from the Centre for Trials Research (contact: esteem@cardiff.ac.uk), subject to approval by the Trial

Management Group (TMG) and Trial Steering Committee (TSC). Data will be fully anonymised. Requests will be considered for scientifically sound proposals addressing questions in line with participant consent and ethical approvals. Access will be provided under a data-sharing agreement. Data will be available from 12 months after publication of the main results for a minimum of 5 years.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	16/09/2025	03/10/2025	No	Yes
Protocol file	version 2.0	01/12/2025	22/01/2026	No	No