ISRCTN18011296 https://doi.org/10.1186/ISRCTN18011296

Use of hormone replacement therapy in the management of chest pain after spontaneous coronary artery dissection in peri and post-menopausal women

Submission date
17/06/2025

Recruitment status
No longer recruiting

Registration date
08/08/2025

Overall study status
Ongoing

Last Edited
25/09/2026

Condition category
Circulatory System

[X] 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
Spontaneous coronary artery dissection (SCAD) is a condition occurring when a bruise appears in the wall of a coronary artery that supplies blood to the heart. This bruise will often heal by itself and does not require stenting (where doctors put a tiny tube inside the affected artery to keep it open and help blood flow smoothly). Prognosis after SCAD is good and the condition is most often managed using medications; however, chest pain after SCAD is very common (we call this post-SCAD chest pain). It is thought to be harmless, but it can be very painful and worrying, and can lead to patients being admitted to the hospital to get checked out. This study is testing whether hormone replacement therapy (HRT) can help reduce chest pain in women who are going through or have gone through menopause and have previously had SCAD. The aim is to see if HRT is a safe and effective treatment for these symptoms and whether a larger study would be possible in the future.

Who can participate?
Women aged 45 or older who are peri- or post-menopausal and have had SCAD in the past three years can take part. They must also be experiencing chest pain on at least four days in the past month. Women who are currently taking HRT, have certain medical conditions (like a history of stroke, cancer, or blood clots), or are pregnant or breastfeeding cannot take part.

What does the study involve?
Participants will be randomly assigned to receive either HRT or a placebo (a dummy treatment) for 12 months. The HRT includes oestrogen gel applied to the skin daily and progesterone capsules taken by mouth. The dose of oestrogen may be increased during the study if chest pain doesn’t improve. Participants will have follow-up checks at 3, 6, and 12 months to assess chest pain, menopausal symptoms, quality of life, and any side effects. They will also use a mobile app to record daily chest pain symptoms.

What are the possible benefits and risks of participating?
Participants may benefit from reduced chest pain and improved menopausal symptoms. The study will also help researchers understand whether HRT is safe for women with a history of SCAD. As with any treatment, there may be side effects. These could include headaches, changes in blood pressure, or rare risks like blood clots or allergic reactions. Participants will be closely monitored throughout the study.

Where is the study run from?
The study is being run from Glenfield Hospital, part of the University Hospitals of Leicester NHS Trust, and managed by the University of Leicester.

When is the study starting and how long is it expected to run for?
June 2025 to July 2027

Who is funding the study?
The study is funded by the National Institute for Health and Care Research (NIHR). Additional support is provided by Besins Healthcare Ireland Ltd., BeatSCAD (a patient charity), and the Leicester NIHR Biomedical Research Centre.

Who is the main contact?
The Chief Investigator is Professor David Adlam, HRTSCAD@leicester.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Prof David Adlam

Contact details
Department of Cardiovascular Sciences (University of Leicester), Glenfield Hospital, Groby Road
Leicester
United Kingdom
LE3 9QP
+44 (0) 0116 2044751
HRTSCAD@leicester.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
1010557

Central Portfolio Management System (CPMS)
75028

Protocol serial number
0995

Study information

Scientific Title
A pilot study of hormone replacement therapy in peri and post-menopausal patients with spontaneous coronary artery dissection and chest pain (HRT-SCAD)

Acronym
HRT-SCAD

Study objectives
To determine the feasibility to recruit and randomise 60 peri- and post-menopausal patients with chest pain after SCAD to either bi-HRT or placebo.

To inform on the proposed efficacy and safety of bi-HRT in the management of post-SCAD chest pain.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/08/2025, North East – Tyne and Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 104 8014; tyneandwearsouth.rec@hra.nhs.uk), ref: 25/NE/0121

Primary study design
Interventional

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

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Post-spontaneous coronary artery dissection (SCAD) chest pain

Interventions
This pilot study is a randomised, double-blind, placebo-controlled trial investigating the feasibility, safety, and potential efficacy of hormone replacement therapy (bi-HRT) in peri- and post-menopausal women aged 45 and over with a history of spontaneous coronary artery dissection (SCAD) and ongoing chest pain. Sixty participants will be randomised in a 1:1 ratio using an Interactive Web Response System (IWRS) with permuted blocks of varying sizes to receive either bi-HRT or matched placebo for 12 months. The active treatment comprises transdermal 17-beta-estradiol (Oestrogel) starting at 2 pumps daily, with potential up-titration to 3 pumps at 3 months and 4 pumps at 6 months if chest pain persists, and oral micronised progesterone (Utrogestan) at 100 mg daily for post-menopausal women or 200 mg daily for 12–14 days per cycle for peri-menopausal women. The placebo arm receives identically administered matched placebos. Follow-up assessments occur at 3, 6, and 12 months and include evaluations of chest pain (via the Seattle Angina Questionnaire-7 and Orbita app), menopausal symptoms, quality of life, psychological wellbeing, medication adherence, and safety monitoring, including adverse events and hospitalisations. The trial is conducted at Glenfield Hospital, Leicester, and aims to inform the design of a future definitive trial.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Utrogestan [Micronised Progesterone], Oestrogel Pump-Pack 750 micrograms/actuation Gel [Oestrogen]

Primary outcome(s)
The following endpoints will be captured at the trial visits relevant to the outcome measure, e. g., baseline (pre-randomisation), 3, 6 and 12 months:
1. Patient eligibility, recruitment and retention, measured using screening logs, randomisation lists and follow-up completion in the electronic case report form (eCRF) via the numbers screened, randomised, withdrawn from the trial and the reasons for trial withdrawal
2. Patient willingness to be consented and adherence to randomised trial treatment, measured using screening logs, randomisation lists, and discontinuation/completion data collected in the eCRF via the numbers withdrawn from the study trial medication and the reasons for trial medication withdrawal
3. Patient acceptability of randomisation and research visits/data collection measured using data completion in the eCRF
4. Completeness of data collection for patient efficacy outcomes throughout the trial [measured using a data source]
5. Compliance and adherence to trial treatment will mostly be measured using patient-reported compliance and adherence, and also via blood and serum measurements of oestrogen hormones and progesterone and hormone metabolites

Key secondary outcome(s)
Efficacy outcomes will be assessed at baseline, 3, 6 and 12 months:
1. Post-SCAD chest pain measured using the Seattle Angina Questionnaire-7 (SAQ-7)
2. Quality of life measured using the Patient Health Questionnaire-9 (PHQ-9), self-reported quality of life using the EQ-5D-5L questionnaire, general self-efficacy scale for psychological assessment, Generalised Anxiety Disorder Assessment (GAD-7), Cardiac Anxiety Questionnaire (CAQ) and Warwick Edinburgh mental wellbeing scale
3. Non-menopausal ‘cardiac’ symptoms (breathlessness, palpitations) measured using data captured via the Orbita app.
4. Hospital admission, adjudicated as MACCE (death, recurrent acute myocardial infarction, recurrent SCAD, revascularisation and stroke), post-SCAD cardiac symptoms and unrelated (including non-MACCE vascular events) by the Data Safety and Monitoring Committee (DSMC), measured using data collected from patient electronic medical records in the eCRF at one timepoint
5. Menopausal symptom severity and frequency measured using a standard, tailored Menopause Symptom Questionnaire
6. Use, or changes in doses, of medications and non-hormonal treatments for menopausal symptoms measured using data collected at follow-up visits in the eCRF at one timepoint

Safety outcomes will be measured using data collected from patient electronic medical records and self-reported by the participant at 3, 6 and 12 months:
1. Hospital admission, adjudicated as MACCE (death, recurrent acute myocardial infarction, recurrent SCAD, revascularisation and stroke), post-SCAD cardiac symptoms or unrelated

(including non-MACCE vascular events)
2. MACCE events
3. New onset breast cancer, endometrial or ovarian cancer
4. Non-fatal thromboembolism
5. Non-MACCE vascular events

Completion date
31/07/2027

Eligibility

Key inclusion criteria
1. Age ≥45 years
2. Confirmed as peri- (from the time of onset of first menstrual irregularity) or post-menopausal (12-consecutive months without a menstrual period)
3. Confirmed previous SCAD on invasive angiography in the 3 years prior to screening
4. Symptomatic chest pain occurring on at least 4 days in the previous 1-month
5. Able to understand written English

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
45 Years

Upper age limit
120 Years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. History of heart failure
2. History of stroke or TIA
3. Previous or known thromboembolic diseases or disorders
4. Previous breast cancer or a family history of breast cancer (1st degree relatives)
5. Recorded allergies to soya or peanut, the trial investigational medical products or excipients
6. Previous endometrial or ovarian cancer
7. Requiring hormonal contraception
8. Has a Mirena coil in situ, or has had a previous hysterectomy
9. Childbirth in the last 12-months and/or breastfeeding at the time of screening

10. Taking HRT in the past 6-months
11. Currently or have in the last 1 month taken another IMP
12. Unable to provide fully informed consent
13. Undiagnosed genital bleeding
14. Untreated endometrial hyperplasia
15. Acute liver disease or a history of liver disease.
16. Any other significant healthcare issue deemed by the research team to have a potential impact on trial outcomes

Date of first enrolment
15/08/2025

Date of final enrolment
15/08/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
-
-
-
England
-

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

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/will be available upon request from Prof Adlam either through the University of Leicester or the HRT SCAD study mailbox, HRTSCAD@leicester.ac.uk. The anonymous datasets based on the outcome measures will be available after the study has been completed and the results have been published for up to 25 years (per archiving requirements). Appropriately trained researchers will be able to request this, subject to approval via our University governance pathways and as per our funder requirements.

IPD sharing plan summary
Available on request