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Reducing the rate of blood clots in patients undergoing varicose vein treatment

Submission date 24/02/2023	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 15/09/2023	**Overall study status** Ongoing	
Last Edited 06/03/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Varicose veins are enlarged veins close to the surface of the skin. They are connected to the bigger deeper veins in the leg, known as deep veins. Endovenous interventions are keyhole operations for varicose veins that are carried out from within the vein itself. Because of this, operations to close the varicose veins can increase the chance of a blood clot forming in the deep veins. Blood clots in the deep veins happen in around 1 in 50 people after endovenous operations. A clot in the leg can cause swelling, pain, and other problems. If a clot in the leg travels to the lungs, it may be life-threatening. Medicines to reduce the blood's tendency to form clots are often prescribed to patients at high risk of blood clots. However, it is unclear if these clot-reducing medicines are beneficial in preventing blood clots in people having these varicose vein procedures. Elastic stockings that squeeze the leg and improve the blood flow through the veins are applied after the varicose vein procedure which helps to reduce the risk of blood clots. This study will investigate if it is worthwhile to prescribe medicines to reduce blood clots after varicose vein procedures. People enrolled in the study will undergo an assessment to make sure that they don’t have the most important risk factors for clots.

Who can participate?
Patients aged over 18 years scheduled to undergo endovenous treatment of varicose veins under local anaesthetic

What does the study involve?
Participants will receive stockings along with, at random, one of the following three treatments:
1. No clot-reducing medicine, or
2. A single dose of clot-reducing medicine, or
3. An extended course (7-14 days) of clot-reducing medicine
Everyone in the study will get an ultrasound scan 21-28 days after their operation to check if they have not developed a blood clot. This scan is not routinely performed in the NHS and is an additional scan to ensure that all blood clots are detected early. Participants will also receive a phone call 7- and 90-days after their procedure to see if they have developed a blood clot or had any problems with the treatment.

What are the possible benefits and risks of participating?
Patients who would not normally be given blood thinning medication as standard treatment may be assigned to the blood thinning medication group and thus may have a lower risk of developing a blood clot. Similarly, patients who would have normally received blood thinning medication and may have experienced an adverse reaction to this treatment may be assigned to the group receiving only elastic stockings, thus reducing the likelihood of potentially experiencing an adverse reaction to the medication. In addition to this, participants in all arms of the trial will be monitored closely for any complications of blood thinners and stockings, so that any complications can be detected and acted upon. Participants will have an extra non-invasive leg scan about 3 weeks after their procedure to detect any asymptomatic blood clots in the legs. Patients not entered into the study would not normally be offered this scan unless they showed symptoms.
The trial will be continually monitored for safety and stopped at any time on the recommendation of the data monitoring committee if there is marked clinical harm resulting in a lack of equipoise and it being deemed unethical to continue the trial. A study-specific risk assessment will also be performed prior to the start of the study by the study sponsor. The risk assessment will consider all aspects of the study and will be updated as required during the course of the study.
We do not expect participation to result in any additional burden on the participant. Participants will attend hospital for a duplex venous ultrasound scan 21 days after the procedure, and the researchers will offer reimbursement for travel. Participants will then be followed up remotely at 7 and 90 days after the procedure. Data can be provided by online survey, text or telephone depending on patient preference. Minimal data collection will occur at these follow-ups.
Incidental findings may be identified during study assessments, such as the duplex ultrasound scan. Such findings will be reported to the local clinical team and to the participant's GP.
Blood thinners are offered routinely to people who would be eligible to participate in this study. Possible complications of blood thinners are bleeding, allergy, rash and low numbers of platelets in the blood (platelets help the blood to clot). These are only the complications which could occur; we are not expecting them all to happen to every participant, and the majority of people do not have any complications. The risk of blood clots is higher in pregnant women. Pregnant women therefore should not take part in this study, and neither should women who plan to become pregnant during the 90 days of the study. Women who could become pregnant should use an effective method of contraception during the course of this study. Any woman who finds that she has become pregnant while taking part in the study should inform her research doctor as soon as possible.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
February 2023 to August 2026

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Sarah Whittley, s.whittley@imperial.ac.uk

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Scientific

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Additional identifiers

EudraCT/CTIS number
2023-000217-40

IRAS number
1007271

ClinicalTrials.gov number
NCT05735639

Secondary identifying numbers
22CX7510, CPMS 55506

Study information

Scientific Title
THRomboprophylaxis in Individuals undergoing superficial endoVEnouos treatment (THRIVE): a multicentre assessor-blind randomized controlled trial

Acronym
THRIVE

Study objectives
Primary objective:
To establish whether patients undergoing endovenous varicose vein interventions benefit from a single dose or an extended course of pharmacological thromboprophylaxis to prevent venous thromboembolism (VTE)

Secondary objectives:
1. Comparisons of quality of life at 7- and 90-days post-procedure using the EQ-5D
2. Mortality rates in each group
3. Cost-effectiveness of providing pharmacological thromboprophylaxis
4. Sub-group analyses of the following risk assessment tools: Department of Health Risk Assessment (DHRA) tool, Caprini score
5. Individual components of the composite outcome

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/09/2023, London - Brent Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)20 7104 8128; brent.rec@hra.nhs.uk), ref: 23/LO/0261

Study design
Randomized controlled open parallel-group trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
VTE prevention (in patients undergoing endovenous varicose vein interventions)

Interventions
Participants (n = 6,660) will undergo 1:1:1 web-based randomization to one of three thromboprophylaxis strategies prior to undergoing endovenous treatment. Randomization will be conducted through an automated system linked to the eCRF setup via the Study Data Centre at the Edinburgh Clinical Trials Unit.

Participants will be individually randomized to one of three thromboprophylaxis strategies prior to undergoing endovenous treatment:
1. Compression therapy alone
2. Compression therapy + a single dose of low-molecular-weight heparin (LMWH) at the time of the procedure
3. Compression therapy + a single dose of LMWH at the time of the procedure + extended prophylactic dose of anticoagulation with LMWH or direct-acting oral anticoagulants (DOAC)

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Dalteparin sodium, enoxaparin sodium, tinzaparin sodium, apixaban, rivaroxaban, dabigatran etexilate

Primary outcome measure
Lower limb deep vein thrombosis (DVT) (with or without symptoms), or pulmonary embolism (PE) with symptoms, assessed using duplex ultrasound and VTE outcome questionnaire (self-reported) at 7 days post-procedure, 21 days post-procedure, and 90 days post-procedure

Secondary outcome measures
1. Lower limb DVT with or without symptoms (individual component of the composite outcome), assessed using duplex ultrasound and VTE outcome questionnaire (self-reported) at 7 days post-procedure, 21 days post-procedure, and 90 days post-procedure
2. PE with symptoms (individual component of the composite outcome), assessed using VTE outcome questionnaire (self-reported) at 7 days post-procedure, and 90 days post-procedure
3. Quality of life measured using EQ-5D at 7 days post-procedure and 90 days post-procedure

4. Mortality measured using a self-reported questionnaire and serious adverse event (SAE) reporting form (if applicable) at 90 days post-procedure
5. Cost-effectiveness of providing pharmacological thromboprophylaxis measured using Incremental Cost-Effectiveness Ratio (ICER) at 90 days post-procedure
6. VTE risk stratification using current risk assessment tools (Department of Health Risk Assessment [DHRA] tool, Caprini score) at baseline and up to 90 days post-procedure

Overall study start date
22/02/2023

Completion date
31/08/2026

Eligibility

Key inclusion criteria
1. Adults (>18 years)
2. Scheduled to undergo endovenous intervention of truncal varicose veins under local anaesthesia
3. Treatment technologies including radiofrequency, laser, mechanochemical, foam sclerotherapy and cyanoacrylate glue

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
6660

Key exclusion criteria
Current exclusion criteria as of 06/03/2025:

1. Clinical indication for therapeutic anticoagulation e.g., atrial fibrillation
2. Previous personal or first-degree relative history of VTE
3. Thrombophilia
4. Female patients of childbearing potential who have a positive pregnancy test
5. A history of allergy to heparins or direct oral anticoagulants
6. A history of heparin-induced thrombocytopenia
7. Inherited and acquired bleeding disorders
8. Evidence of active bleeding
9. Concomitant major health problems such as active cancer and chronic renal and/or liver impairment

10. Known thrombocytopenia (platelets known to be less than 50 x 10^9/l)
11. Major trauma or non-venous surgery that required local risk assessment for VTE in the previous 90 days
12. Recent ischemic stroke in the previous 90 days
13. Inability to provide consent

Previous exclusion criteria as of 12/01/2024:

1. Clinical indication for therapeutic anticoagulation e.g., atrial fibrillation
2. Previous personal or first-degree relative history of VTE
3. Thrombophilia
4. Female patients of childbearing potential who have a positive pregnancy test
5. A history of allergy to heparins or direct oral anticoagulants
6. A history of heparin-induced thrombocytopenia
7. Inherited and acquired bleeding disorders
8. Evidence of active bleeding
9. Concomitant major health problems such as active cancer and chronic renal and/or liver impairment
10. Known thrombocytopenia (platelets known to be less than 50 x 10^9/l)
11. Surgery or major trauma in the previous 90 days
12. Recent ischemic stroke in the previous 90 days
13. Inability to provide consent

Previous exclusion criteria:

1. Clinical indication for therapeutic anticoagulation
2. Clinical contraindication to anticoagulation
3. Previous personal or family history of VTE
4. Thrombophilia
5. Inability to provide informed consent or consent by personal/professional legal representative
6. A positive test for SARS-CoV2 <3 months of procedure
7. Female patients of childbearing age who have a positive pregnancy test

Date of first enrolment
15/01/2024

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Wales

Study participating centre
Aneurin Bevan University Health Board
Lodge Road
Caerleon
Newport
United Kingdom
NP18 3XQ

Study participating centre
Brighton and Sussex University Hospitals NHS Trust
Royal Sussex County Hospital
Eastern Road
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BN2 5BE

Study participating centre
Buckinghamshire Healthcare NHS Trust
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Study participating centre
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CB2 0QQ

Study participating centre
Cardiff & Vale University Lhb
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CF14 4HH

Study participating centre
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CF37 1LB

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Sponsor type
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ROR
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Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website

This trial will lead to publications in peer reviewed journals alongside presentations at international academic conferences including European and American vascular, venous, general surgery and haematology societies. The results may influence recommendations for NICE guidelines in reference to endovenous procedures in the treatment for varicose veins and also VTE prevention in addition to recommendations European Society for Vascular Surgery guidelines on chronic venous disease. Furthermore, the cost-effectiveness information may guide clinical commissioning groups and NICE in the provision of thromboprophylaxis strategies. From a wider scientific perspective, the trial will lead to a greater understanding of the safety for 10-day courses of pharmacological thromboprophylaxis strategies and will likely stimulate updates to systematic review of literature and meta-analyses.

Intention to publish date
31/08/2027

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.0	18/08/2023	15/09/2023	No	No
Protocol article		17/02/2024	19/02/2024	Yes	No