ISRCTN11667770 https://doi.org/10.1186/ISRCTN11667770

A randomised controlled trial investigating the effects of compression stockings in patients who require blood thinning medication post discharge from elective surgery

Submission date
15/12/2023

Recruitment status
Recruiting

Registration date
18/12/2023

Overall study status
Ongoing

Last Edited
09/07/2025

Condition category
Circulatory System

[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
Hospital-acquired thrombosis (HAT) is defined as any venous thromboembolism (VTE) within 90 days of hospital admission, encompassing both deep vein thrombosis (DVT) and pulmonary embolism (PE). HAT represents a significant cause of preventable death, with over 12,000 people dying each year from hospital-associated VTE in the UK. Previous studies report that the risk of untreated high-risk surgical patients developing HAT is as high as 40-60% in orthopaedic patients and 15-40% in general surgery patients. For these patients at highest risk of VTE, key prevention strategies include extended pharmacological thromboprophylaxis (EDPTP) prescribed beyond hospital discharge and provision of graduated compression stockings (GCS). There is compelling evidence to support the use of pharmacological thromboprophylaxis, however, there is little evidence to support the use of additional GCS, which can cause complications in as many as 5% of patients. Providing GCS in this group costs the NHS a minimum of £8.3 million per annum. This study aims to establish whether:
1. Patients undergoing surgical procedures requiring EDPTP benefit from additional GCS to prevent VTE
2. Patients receiving GCS experience an increased rate of adverse events

Who can participate?
Patients aged 18 years or older undergoing elective surgery and requiring extended duration (post-discharge) blood thinning medication who have not been advised not to take blood thinners or wear GCS

What does the study involve?
Participants will be randomly allocated to one of two thromboprophylaxis strategies:
1. EDPTP* in addition to GCS, or
2. EDPTP alone and followed up for 90 days post-surgery.
Participation in the study will last 3 months from entry. Participants will be contacted at three time points post-surgery (7 days, between 21 and 35 days and 90 days later) to ask some

questions about their health and how often they have worn their stockings and taken blood thinners. The questions can be answered via telephone or an online survey (the link to this survey will be sent via email or text message). Participants will also be invited back to the hospital between 21 and 35 days to have an additional scan of the veins in their legs to detect any blood clots that may have developed.

What are the possible benefits and risks of participating?
Side effects of elastic stockings are uncommon. Whilst the researchers do not anticipate any specific side effects as a result of taking part in this trial, in rare circumstances, some patients may be allergic to the materials that are contained within the stockings. Furthermore, some people find the stockings uncomfortable to wear but this causes no lasting effects. Very rarely the compression stockings can cause abrasions of the skin. The researchers are uncertain if wearing stockings reduces the chances of a blood clot developing which is why they are organising this study. Participants be provided with a leaflet which explains how to recognise the signs and symptoms of a blood clot. The duplex ultrasound is designed to detect any asymptomatic DVTs.

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

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

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

Who is the main contact?
Dr Francine Heatley, f.heatley@imperial.ac.uk

Study website
https://shorturl.at/gGOZ7

Contact information

Type(s)

Contact name
Miss Francine Heatley

ORCID ID
https://orcid.org/0000-0002-5184-0259

Contact details
Room 3
4th Floor East Wing
Charing Cross Hospital
-
United Kingdom
W6 8RF
-
f.heatley@imperial.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
333539

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 60092, IRAS 333539

Study information

Scientific Title
Graduated compression stocking as an adjunct to extended duration pharmacological thromboprophylaxis for venous thromboembolism prevention

Study objectives
The use of graduated compression stockings (GCS) in addition to giving blood thinning medication post-discharge from hospital for surgical patients at the highest risk of venous thromboembolism (VTE) is non-inferior to giving blood thinning medication alone.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/12/2023, Wales REC 3 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0) 2922 941107; Wales.REC3@wales.nhs.uk), ref: 23/WA/0350

Study design
Randomized; Interventional; Design type: Prevention, Management of Care, Surgery

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet

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

Health condition(s) or problem(s) studied
Venous thromboembolism

Interventions
Baseline Visit (Visit 0):
Consenting participants will be randomised in a 1:1 fashion to one of two thromboprophylaxis strategies:
1. Extended duration pharmacological thromboprophylaxis (EDPTP)* in addition to GCS (control arm), or
2. EDPTP alone (intervention arm)
*EDPTP includes any anti-thrombotic agent prescribed at a prophylactic dose for prevention of VTE, including low-molecular-weight heparin (LMWH), Directly acting Oral AntiCoagulants (DOACs), or antiplatelet therapy. Participants are deemed to require extended duration thromboprophylaxis measures as per local policy in line with NICE [NG89] guidelines. Examples of procedures from which patients are at the highest risk of VTE include (but are not limited to): orthopaedic surgery (total hip replacement, total knee replacement, colorectal surgery (colectomy, splenectomy), upper gastrointestinal surgery (oesophagectomy, gastrectomy), urological surgery (cystectomy, nephrectomy), and gynaecological oncology surgery (radical hysterectomy, radical trachelectomy).

Intervention arm:
Participants randomised to the intervention arm will receive EDPTP alone post-surgery (no GCS). Extended-duration pharmacological thromboprophylaxis is the practice of prescribing thromboprophylaxis for a duration after hospital discharge. Prevention of DVT is a licenced indication and recommended by NICE guidelines [NG89] for several Low molecular weight heparins (LMWH) such as tinzaparin, enoxaparin, or direct oral anticoagulants (DOACs) such as rivaroxaban, apixaban. Aspirin is an antiplatelet medication that reduces platelet function with a variety of clinical indications. The use of aspirin as DVT prophylaxis in orthopaedic surgery is also recommended by NICE [NG89]. Prophylactic-dose thromboprophylaxis is prescribed at a lower dose in comparison to clinical indications for therapeutic anticoagulation, such as in the treatment of diagnosed DVT or PE.

Control arm:
Participants randomised to the control arm will receive both EDPTP and GCS for a period of time post-discharge as per local policy which may vary between Trusts.
GCS are elastic stockings worn on the lower limbs, often referred to by one of the brand names ThromboEmbolic Deterrent (TED®) stockings. They provide low-pressure compression with the intended benefit of reducing the risk of VTE.

Prior to the surgical procedure, all participants will be provided with a leaflet which explains the signs and symptoms of developing a blood clot. Although VTE outcome will be assessed at 7, 21 to 35 days and 90 days post-procedure, participants will be advised to visit the emergency department if they suspect they have developed a blood clot (and not to wait for the study team to make contact).

Prior to the surgery, the following information will be collected from the patient and medical records:
1. Baseline demographic information

2. Name of surgical procedure
3. Previous medical history and current medication

Follow-up:
Participants will be contacted by the central study team at days 7, between 21 and 35 days, and 90 days to obtain follow-up data. The follow-up will be conducted either by telephone, SMS or web depending on participant preference. Participants will undergo a full lower limb DVT scan at 21-35 days post-intervention to identify asymptomatic DVT, this is timed to capture the peak onset of events which is at 3 weeks.

Day 7 post-procedure:
Day 7 post procedure (data collected via telephone or online survey [link to survey sent via email or SMS])
1. VTE outcome (participants will be asked to report on whether or not they have been diagnosed with a DVT or PE within the past 7 days)
2. Adverse events associated with GCS will be captured (for those enrolled in the control arm)
3. Participant reported adherence to GCS (for those enrolled in the control arm)
4. Participant reported adherence to EDPTP

Day 21 to 35 post-procedure:
Day 21 to 35 post-procedure (data collected via telephone or online survey [link to survey sent via email or SMS])
1. VTE outcome (participants will be asked to report on whether or not they have been diagnosed with a DVT or PE within the past 7 days)
2. Adverse events associated with GCS will be captured (for those enrolled in the control arm)
3. Participant reported adherence to GCS (for those enrolled in the control arm)
4. Participant reported adherence to EDPTP
5. Participants will also undergo a full lower limb DVT scan at 21- 35 days post-intervention to identify asymptomatic DVT

Day 90 post-procedure:
Day 90 post procedure (data collected via telephone or online survey [link to survey sent via email or SMS])
1. VTE outcome (participants will be asked to report on whether or not they have been diagnosed with a DVT or PE within the past 7 days)
2. Adverse events associated with GCS will be captured (for those enrolled in the control arm)
3. Participant reported adherence (for those enrolled in the control arm)
4. Participant reported adherence to EDPTP
Mortality within the 90-day follow-up period will also be captured. Follow-up data will be assessed blinded

Intervention Type
Mixed

Primary outcome measure
Imaging-confirmed lower limb DVT with or without symptoms, or PE with symptoms, occurring up to 90 days post-surgery

Secondary outcome measures
Defined as occurring within 90 days of surgery:
1. Mortality recorded within 90 days

2. Adverse events related to GCS recorded within 90 days
3. Adherence with GCS, defined as (percentage of actual days worn / maximum number of days prescribed according to local practice)
4. Adherence with EDPTP, defined as (percentage of actual days taken / maximum number of days prescribed, according to local practice)
5. Safety outcome measures, defined as major bleeding events recorded within 90 days

Overall study start date
13/04/2023

Completion date
30/09/2026

Eligibility

Key inclusion criteria
1. Adults (>18 years)
2. Participants undergoing elective surgery; risk assessed as requiring EDPTP. Participants are deemed to require extended duration thromboprophylaxis measures as per local policy in line with NICE [NG89] guidelines. Examples of procedures from which patients are at the highest risk of VTE include (but are not limited to): orthopaedic surgery (total hip replacement, total knee replacement, colorectal surgery (colectomy, splenectomy), upper gastrointestinal surgery (oesophagectomy, gastrectomy), urological surgery (cystectomy, nephrectomy), and gynaecological oncology surgery (radical hysterectomy, radical trachelectomy).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 8608; UK Sample Size: 8608

Key exclusion criteria
1. Contraindications to EDPTP or GCS
2. Individuals requiring therapeutic anticoagulation e.g., anticoagulation for previous DVT
3. Known thrombophilia or thrombogenic disorder

Date of first enrolment
01/05/2024

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Barnsley Hospital NHS Foundation Trust
Gawber Road
Barnsley

United Kingdom
S75 2EP

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Sherwood Forest Hospitals NHS Foundation Trust
Kings Mill Hospital
Mansfield Road
Sutton-in-ashfield
United Kingdom
NG17 4JL

Study participating centre
Northern Care Alliance NHS Foundation Trust
United Kingdom
M6 8HD

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
The Rotherham NHS Foundation Trust
Moorgate Road
Rotherham
United Kingdom
S60 2UD

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
Cheltenham General Hospital
Sandford Road
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
Portsmouth Hospitals University NHS Trust
Queen Alexandra Hospital
Southwick Hill Road
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
South Tyneside and Sunderland NHS Foundation Trust
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Royal National Orthopaedic Hospital NHS Trust
Brockley Hill
Stanmore
United Kingdom
HA7 4LP

Study participating centre
Royal Cornwall Hospitals NHS Trust
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LJ

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Lewisham and Greenwich NHS Trust
University Hospital Lewisham
Lewisham High Street
London
United Kingdom
SE13 6LH

Study participating centre
Southern Health and Social Care Trust
Southern Area College of Nursing
Craigavon Area Hospital
68 Lurgan Road, Portadown
Craigavon
United Kingdom
BT63 5QQ

Study participating centre

Royal Surrey County Hospital NHS Foundation Trust
Egerton Road
Guildford
United Kingdom
GU2 7XX

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Blackpool Teaching Hospitals NHS Foundation Trust
Victoria Hospital
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Ashford and St. Peter’s Hospitals Trust
United Kingdom
KT16 0PZ

Study participating centre
St George's University Hospitals NHS Foundation Trust
United Kingdom
SW17 0QT

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Queen Victoria Hospital NHS Foundation Trust
Holtye Road
East Grinstead
United Kingdom
RH19 3DZ

Study participating centre
Northern Lincolnshire and Goole NHS Foundation Trust
Diana Princess of Wales Hospital
Scartho Road
Grimsby
United Kingdom
DN33 2BA

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
North Cumbria Integrated Care NHS Foundation Trust
Pillars Building
Cumberland Infirmary
Infirmary Street
Carlisle
United Kingdom
CA2 7HY

Study participating centre
The Cleveland Clinic
United Kingdom
SW1X 7HY

Study participating centre

Mid Yorkshire Teaching NHS Trust
Pinderfields Hospital
Aberford Road
Wakefield
United Kingdom
WF1 4DG

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Mid and South Essex NHS Foundation Trust
Prittlewell Chase
Westcliff-on-sea
United Kingdom
SS0 0RY

Study participating centre
Swansea Bay University Local Health Board
Tonna Hospital
Tonna Uchaf
Tonna
Neath
United Kingdom
SA11 3LX

Sponsor information

Organisation
Imperial College London

Sponsor details
Research Governance and Integrity Team
Room 217, Level 2, Medical School Building
Norfolk Place
London

England
United Kingdom
W2 1PG
+44 (0)20 7594 9480
cheuk-fung.wong@imperial.ac.uk

Sponsor type
University/education

Website
http://www.imperial.ac.uk/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR155294

Results and Publications

Publication and dissemination plan
The following outputs are anticipated to arise from the GRACE trial by 30th March 2028:
1. Publications in peer-reviewed journals (including the protocol paper and main trial analysis)
2. The NICE guidelines aiming to prevent VTE “Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism [NG89]” will be subsequently updated
3. Cost-effectiveness information to guide clinical commissioning groups and NICE
4. Updated systematic review of literature and meta-analysis
5. An understanding of the safety of GCS and subsequent quality of life
6. Presentation at international academic conferences including European and American vascular, venous, general surgery and haematology societies
7. The results of the trial will be emailed to participants and published through patient groups such as Thrombosis UK
8. Dissemination of results to the wider public through social media streams
9. If GCS are found to ineffective, this could prompt a wider effect on the design and application of graduated compression stocking devices within the healthcare setting

Intention to publish date
30/03/2028

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 article		06/07/2025	08/07/2025	Yes	No