

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 18/12/2023	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 17/04/2024	Condition category Circulatory System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English Summary

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 September 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

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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 hypothesis

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

Condition

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

Overall study end date

30/09/2026

Eligibility

Participant 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

Participant 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

Recruitment start date

01/05/2024

Recruitment end date

30/06/2026

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Charing Cross Hospital

Fulham Palace Road

London

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W6 8RF

Study participating centre

St Mary's Hospital

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Sponsor information

Organisation

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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 be 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