



Synopsis

Compression Hosiery to Avoid the Post-Thrombotic Syndrome: a synopsis of the CHAPS RCT

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Abstract

Background: Approximately half of adults diagnosed with deep vein thrombosis will develop the post-thrombotic syndrome leading to chronic symptoms – including leg pain, oedema, venous ectasia and, in 5% of cases, venous ulceration. Risk factors include older age, obesity, a history of blood clots, cancer and heart failure. Despite adequate anticoagulation, post-thrombotic syndrome remains a chronic health condition with significant financial burden for patients and health services.

The effectiveness of compression stockings in preventing post-thrombotic syndrome is unclear and whether the risks and costs associated with compression stockings are justified.

Design: The Compression Hosiery to Avoid Post-Thrombotic Syndrome study was a multicentre, pragmatic, assessor-blind, randomised controlled trial of adults with a first proximal deep vein thrombosis.

Setting: Secondary care National Health Service hospitals in the United Kingdom.

Participants: Patients ≥ 18 years, with imaging-confirmed, symptomatic presentation of first deep vein thrombosis in the lower limb (popliteal, femoral, iliac or combination), ≤ 3 weeks from diagnosis.

Interventions: Participants were randomised 1 : 1 to standard care (anticoagulation as per local guidelines) or intervention (anticoagulation as per local guidelines and regular use of a graduated compression stocking).

Primary outcome: The primary outcome was any incidence of post-thrombotic syndrome using the Villalta criteria over a median of 18-month follow-up (range 6–30 months). This was planned to be assessed on up to three occasions (6 and 12 months post randomisation and at study end), depending on when an individual was randomised.

Secondary outcomes: Planned secondary outcomes:

- incidence of venous ulceration (measured by the validated Villalta criteria)
- employment status (change in the number of days working from baseline)
- change in disease-specific and generic quality of life – Venous Insufficiency Epidemiological and Economic Study (VEINES-QOL/Sym) and EuroQol-5 Dimensions scales from baseline over 6 months, 12 months and end of study visit
- adherence to stockings and anticoagulants (patient self-report)
- cost-effectiveness of stocking prescription – incremental cost-effectiveness ratio from the EuroQol-5 Dimensions questionnaire, with appropriate sensitivity analysis.

Results: The trial closed early due to poor recruitment during the COVID-19 pandemic; and, of the planned sample size of 864, 152 participants were randomised. Post-thrombotic syndrome occurred in 51% of the control arm and in 30% of the intervention arm at last follow-up. No serious adverse events relating to stockings were recorded. Stocking adherence was a mean of 6 days (standard deviation 2) per week.

Conclusions: The sample size was not reached, which precluded any formal statistical analysis. Although a difference in the incidence of post-thrombotic syndrome was demonstrated, the effect size could not be determined. There is

interest in understanding optimal strategies for the prevention of post-thrombotic syndrome in these patients and a re-run of this trial should occur.

Limitations: The main limitation was its early termination. As a result, it did not reach the required sample size to draw any adequately powered conclusions. The analyses are descriptive and therefore we cannot determine whether there were any differences between trial arms.

Future work: Answering the question of whether graduated compression stockings help prevent the post-thrombotic syndrome is important to both patients and clinicians.

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Introduction

The aim of this synopsis is to describe the Compression Hosiery to Avoid Post-Thrombotic Syndrome (CHAPS) trial, discuss why the study was terminated early and reflect on how this research might develop in the future. The barriers encountered during the trial are discussed, as well as the current conclusions and future recommendations. Other researchers planning a similar study would benefit from being aware of such barriers and their potential impact.

Rationale for research

There is a lack of evidence for the benefit of graduated compression stockings (GCS) in the prevention of post-thrombotic syndrome (PTS). GCS continue to be prescribed to some patients in the UK after deep venous thrombosis (DVT) without any robust evidence supporting their current use, hence the need for a properly conducted randomised controlled trial (RCT). The CHAPS trial is crucial as it will support future guidance and policy in PTS prevention and will have national and international impacts. This study was also designed to include a primary health economic objective to calculate the cost-effectiveness with regards to the use of GCS in patients diagnosed with DVT.

Background

Deep venous thrombosis occurs in approximately 1–2 per 1000 adults in the UK,¹ and just under half will go on to develop lifelong disability from PTS.² PTS is defined as 'chronic venous symptoms or signs secondary to deep vein thrombosis', for example, lifelong leg pain, oedema and skin changes, progressing in 5% to venous ulceration.³ The pathophysiology of PTS is sustained venous hypertension from venous outflow obstruction and valvular incompetence.⁴ Three clinical scales are widely used to diagnose PTS after objectively diagnosed DVT: Brandjes scale,⁵ Ginsberg measure⁶ and Villalta scale,⁷ with the

Villalta considered as the 'gold standard' for the diagnosis and classification of PTS.⁸ The average age of patients developing PTS is 55 years,⁹ meaning that around half of patients work. Of patients having a lower limb DVT, around 30% of patients will develop mild PTS, 10% moderate and 5% severe PTS.^{2,9} Why some patients with DVT go on to develop PTS is not well understood. The physiological process that lead to PTS is a combination of sustained venous hypertension due to the thrombotic obstruction as well as reflux due to valvular incompetence.⁴

The incidence of DVT rises markedly with age,¹ and the severity of PTS increases with age and high body mass index (BMI).² The future burden of PTS is likely to rise in the UK with an increasingly older and heavier population.

Graduated compression

Graduated compression stockings are elasticated garments and a frequently used therapy for conditions, including varicose veins, lymphoedema, leg ulceration, venous ulcers and the PTS. The exact mechanism of action of GCS is unclear, but they are thought to aid the calf muscle pump to return venous blood back to the heart by exerting higher pressure around the ankle that gradually decreases towards the knee.

In general, GCS are safe to use in most people, but they can cause problems if not properly fitted. Patients who are allergic to the stocking fabric may experience contact dermatitis, skin blisters or skin discolouration. In patients with poor arterial flow, compression can worsen existing ischaemia.¹⁰

In the UK, for patients with proximal DVT, National Institute for Health and Care Excellence recommends wearing below-knee GCS with pressure > 23 mmHg (at the ankle) for at least 2 years, beginning a week after diagnosis or when swelling is reduced sufficiently, and if there is no contraindication.¹¹ The recommendation was based on evidence from two RCTs.^{5,12} Both studies found that about half of the patients with a first episode of proximal DVT had PTS within 2 years, and GCS

decreased this rate by about 50%. These studies showed a clinically important reduction in the incidence of PTS [254 fewer per 1000, 95% confidence interval (CI) 172 to 311 fewer], although there were no comparative data on adverse events.¹³

A meta-analysis of five RCTs showed that severe PTS occurred in 5% of patients given GCS and 12% of patients with no compression (relative risk 0.38, 95% CI 0.22 to 0.68). PTS of any severity occurred in 26% with stockings and in 46% without stockings (relative risk 0.54, 95% CI 0.44 to 0.67).¹⁴

Objectives

The CHAPS aimed to measure the difference in incidence of PTS at a median of 18-month follow-up after first, acute DVT between standard clinical care (anticoagulation) and the intervention arm [a graduated compression stocking and the standard clinical care (anticoagulation)].

Secondary objectives were:

- to compare the specific and generic quality of life at the end of the trial
- to compare employment status at the end of the trial
- to evaluate whether the use of stockings to prevent PTS is cost-effective
- to perform a detailed process evaluation to understand barriers to adherence
- to measure adherence in detail over the initial first year and at the end of the trial
- to capture off-label stocking use in the standard care arm.

Methods

Trial design

The CHAPS was a UK, multicentre, assessor-blind, pragmatic RCT. A process evaluation was designed to complement the main CHAPS trial, with the aim to understand the efficacy of the educational components of the intervention.

The full protocol was published in the *British Medical Journal*.¹⁵ It details the aims, design and planned analyses of the CHAPS trial. Following amendments to the study, an updated protocol paper was published to announce and promote the study to potential European sites.¹⁶

Eligibility criteria

Adults with a first, proximal DVT were eligible to join the trial.

Randomisation

Participants were electronically randomised 1:1 to receive either:

1. standard care – anticoagulation alone
2. intervention – anticoagulation plus GCS.

Study assessments

Baseline

Following consenting and screening procedures, the following baseline measures were captured:

- demographic data – date of birth, gender and ethnicity
- employment status
- height, weight and BMI
- lifestyle data – smoking status, alcohol consumption and physical activity level
- Comprehensive Classification System for Chronic Venous Disorders score
- Villalta's score
- medical history
- concomitant medication
- quality-of-life assessments – EQ-5D-5L, Venous Insufficiency Epidemiological and Economic Study (VEINES-QoL/Sym) and The Brief Illness Perception Questionnaire (B-IPQ).

Study compression

All stockings used in the CHAPS trial were RAL CCL2, manufactured by Medi UK (Hereford, UK). The compression provided by this variety of stocking is 23–32 mmHg at the ankle, reducing as the leg widens to provide 70% of ankle pressure at the knee. The stockings come with a 6 months guarantee of daily wear.

Following a training session, a consignment was provided to each recruiting site. Seven sizes were provided in two lengths: standard fit and petite. Standard length was also provided in extra wide calf, as the calf can often be distorted in patients with DVT. We were guided in the composition of the consignments by Medi's most frequent sales across the UK. It was felt that a wide variety of choice would provide the patient with the highest level of comfort and improve compliance with the garment. Medi were able to provide made-to-measure garments for patients who did not fit into the stock provided.

Stocking fitting and training

The Clinical Trainer at Medi UK provided the nurses responsible for recruiting patients with a stocking training session. Measuring tapes and charts were sent to teams prior to the training session and a Microsoft PowerPoint®

(Microsoft Corporation, Redmond, WA, USA) presentation was provided remotely via Microsoft Teams (Microsoft Corporation, Redmond, WA, USA). The training covered how to measure the participant's legs for the correct size, a demonstration of stocking application and removal and a demonstration of the Medi Butler donning aid. Following consenting procedures, the research nurse measured the participants affected leg for study stockings in the following steps:

1. Ankle circumference was recorded just above the medial and lateral malleolus.
2. Calf circumference was recorded around the widest part of the calf when the participant was sitting or standing.
3. Leg length was measured from two fingers below the hollow of the knee to the floor.

If the participant was between sizes on the sizing chart, a clinical judgement was made. For example, if the leg was swollen at the time of measuring, the smaller acceptable size was chosen based on a predicted reduction in swelling, whereas if the patient dexterity was poor, a larger size may be chosen to ease application.

Follow-up

It was planned that participants in both arms should be followed up face to face at 6 months, 12 months and at a final study visit (between 18 and 30 months, depending on when the patient was recruited into the trial). The intention was to perform visits in clinic so that a blinded clinical assessment of both legs could be performed using the Villalta's score. This was amended during the pandemic, and blinded video calls replaced face-to-face visits to reduce the spread of COVID-19. Participants randomised to receive stockings were additionally contacted at 2 weeks post randomisation. The research nurse discussed any barriers to wearing the stockings, their fit and feel and provided a donning or doffing aid if required.

The following questionnaires were administered to participants in both arms. The frequency of administration is shown in [Appendix 1, Figure 1](#).

- Beliefs about Medicines Questionnaire (BMQ)
- Treatment Intrusiveness Questionnaire (TIQ)
- Brief Illness Perceptions Questionnaire (BIPQ)
- Beliefs about Stockings Questionnaire (BSQ).

Participants randomised to the stocking arm also received a monthly online stocking usage questionnaire:

- Stockings Adherence Reporting Scale.

Blinding

An independent researcher at each site (blind to the treatment allocation) performed leg assessments, including the Villalta's scale. Participants were requested to remove their stockings prior to their clinic visit or video call. They were also reminded not to discuss their treatment allocation with the blinded individual.

End-point assessment

The Villalta scale is generally considered as the 'gold standard' for the diagnosis and the classification of severity of PTS.⁸ The Villalta scale has good inter-rater reliability and correlates with other quality-of-life scores.¹⁷ An independent assessor, trained to use the Villalta scale, determined the presence of PTS.

Sample size calculation

The sample size calculation was based on the primary end point of incidence of PTS. Since the 2014 Compression Stockings to Prevent the Post-Thrombotic Syndrome (SOX) trial, improvements had been made in anticoagulation, and it was anticipated that 30% of the control arm would develop PTS at some point during the follow-up (median 18 months, range 6–30 months) rather than the 40% observed in SOX. In smaller trials, the number needed to treat (NNT) varied from 1 in 2⁵ to 1 in 4;¹² however, SOX demonstrated no benefit. Smaller trials may overestimate treatment effect, so the NNT for CHAPS was set at 1 in 10.

With 864 participants, the study had 90% power at a 5% level of significance, using a test of binomial proportions to detect an absolute reduction in the incidence of PTS of 10% (from 30% in the standard care arm to 20% in the stockings plus standard care arm), allowing for 10% loss to follow-up.

Trial sites and study duration

Sites were selected to take part in CHAPS based on their predicted ability to recruit and the credentials of the local principal investigator. Initially, 11 sites were deemed sufficient to recruit the sample size, but after the COVID-19 pandemic, it became clear that many more sites would need to be brought on board due to capacity and delivery issues across the NHS.

Twenty-seven sites were identified, and site initiation visits were conducted; all received the green light to recruit.

Further sites submitted expressions of interest to take part in the study, including sites across Europe, Russia and the USA.

Ethics

The National Research Ethics Service granted ethical approval from London Bloomsbury Research Ethics Committee (Reference 19/LO/1585).

Results

Over the recruitment period, 2332 participants were screened to take part in the study, of whom 152 were randomised. Seventy-six participants were randomised to receive anticoagulation alone (control group), and 76 were randomised to receive anticoagulation plus a graduated compression stocking (intervention). The total number of participants randomised into the study was significantly below the planned sample size of 864, thus precluding any of the formal planned data analyses described in version 1.0 of the statistical analysis plan (SAP), or detection of a significant difference between the control arm and the treatment arm of the study. The final analysis was still intention to treat and used statistical models to estimate the relevant treatment effects, but the statistical reporting was entirely descriptive (e.g. including 95% CIs but not including any *p*-values from tests of hypothesis). In addition, sensitivity analyses around missing data assumptions were removed from the updated SAP.

Useable data were gathered from 56 participants in the intervention arm and from 55 in the control arm. The sample size for CHAPS was based on the primary end point of any incidence of PTS. PTS occurred in 28/55 (51%) of control arm and in 17/56 (30%) of the intervention arm at last follow-up. No serious adverse events relating to stocking use were recorded. Stocking adherence as reported by participants was a mean of 6 days (standard deviation 2) per week. Sixty per cent of patients wore stockings for > 8 hours per day.

Screening data summary

Patients were screened from secondary care vascular and haematology clinics as well as directly from accident and emergency and ambulatory care at each recruiting site. The main reasons for non-enrolment included pressures arising from the COVID-19 pandemic, clinician decision (e.g. isolated DVT below the popliteal vein) and patient decision. Further details can be found in the supplementary material of the results publication.¹⁸

Baseline data summary

Analysis in the form of descriptive statistics were carried out for data in both arms of the study following database lock.

Health economic analysis and process evaluation

As the trial did not recruit sufficient participants, the Health Technology Assessment agreed that it was not

possible to conduct the health economic analysis or the process evaluation.

Discussion

The principal findings show that the incidence of PTS was lower in the intervention arm (anticoagulation plus a graduated compression stocking) than the control arm (anticoagulation alone). CHAPS demonstrates that a large-scale RCT examining the benefits of stockings versus anticoagulation alone is feasible under normal conditions. Participants will wear compression with supportive encouragement and an appropriately designed intervention. There is interest from both the UK and international scientific community in conducting a re-run of this trial with a slimmed down, efficient design.

Challenges and limitations

COVID-19 pandemic

In December 2019, a case of a novel COVID was identified in Wuhan, China. This highly contagious disease caused by a virus, the severe acute respiratory syndrome coronavirus 2, quickly spread across China, then rapidly across the world. On 30 January 2020, The World Health Organization declared a public health emergency of international concern and a pandemic on 11 March 2020. By summer 2022, the COVID-19 pandemic, as it became known, had led to 6.37 million confirmed deaths, making it one of the deadliest in history.

In the UK, on 16 March 2020, Prime Minister, Boris Johnson, announced that it was time to stop non-essential travel and contact and, on 23 March 2020, he announced the first UK lockdown, ordering people to 'stay at home'. For CHAPS, this meant that all scheduled follow-up visits were paused or conducted remotely via a video link where possible. Sites were asked to stop recruiting new patients into the trial until further notice. A second lockdown across England was announced by the Prime Minister on 31 October 2020 to prevent a 'medical and moral disaster' for the NHS. The third and final lockdown across England occurred on 6 January 2021, with the same restrictions in place as the first lockdown, people stayed at home. These restrictions began to be lifted in March 2021, and a phased exit from lockdown was commenced, which intended to 'cautiously but irreversibly' ease lockdown restrictions.¹⁹ For the CHAPS trial, this meant that recruitment was paused across all sites for around 14 months, as further lifting and implementing of restrictions occurred across 2020 and 2021 in response to different strains of the virus overwhelming hospital services. During this period, most non-front-line nursing staff were redeployed to COVID

wards, and many underwent rapid retraining in intensive care medicine.

The National Institute for Health and Care Research (NIHR), understanding the unprecedented situation faced by almost every sector of business and society, agreed to allow CHAPS to continue. From April 2021, most recruiting sites had officially reopened following suspension. However, over the next 4 months, only five participants were randomised per month on average, vastly behind the predicted targets. In August 2021, a total of 10 participants were randomised. Sites consistently reported issues with staffing (e.g. limited resources, redeployment, the prioritisation of clinical duties and staff leaving teams altogether). As such, participating sites were recruiting at a much slower rate than during normal conditions. At the time, feedback from the study teams suggested that the capacity would improve by the latter part of 2021 into the first quarter of 2022. New sites were activated to assist the drive in recruitment, and by 31 December 2021, it was anticipated that at least 20 sites would be open and recruiting to CHAPS (10 more than originally planned).

Recovery strategies

In April 2022, the study team presented an Options Appraisal to the funder to demonstrate several different scenarios, whereby the trial might reach prespecified milestones and finish on time and to target:

- *Exploration of international sites:* The co-ordinating centre received expressions of interest from 13 international sites. These sites completed a feasibility questionnaire in which they anticipated an ability to recruit, on average, four to five participants per month. Only sites with similar health contexts and settings generalisable to the UK were presented in the Options Appraisal. This option would avoid early closure or significant further delays following the COVID-19 pandemic. Simultaneously, it would develop the international reach of the trial and enable the understanding of shared international priorities and opportunities. Five sites across Russia and Ukraine previously expressed interest, but these requests were not presented due to the unstable geopolitical climate.
- *Exploration of patient identification centres:* The co-ordinating centre liaised with the primary care network to discuss how general practice may assist in patient identification and consent
- *Inclusion of patients with distal DVT:* At the time of the Options Appraisal, around 10% of patients were screened ineligible due to the presence of a distal

DVT, indicating major scope for improving recruitment rates. Distal DVT, in which thrombosis occurs below the popliteal veins, is considered by some as an altogether more benign clinical entity, but it is more common than proximal DVT.²⁰ Nearly 50% of DVTs are distal in origin and, though the odds of developing PTS are lower than with proximal DVT, the authors conducted a systematic review and meta-analysis to define the rate of PTS after distal DVT. This review established that the incidence of PTS in patients with distal DVT is between 15% and 20%.²¹

Following the Options Appraisal meeting and regular monitoring calls with the funder, the NIHR decided that the trial would not meet the revised recruitment targets and took the decision to close the study with immediate effect. Recruitment ceased across all centres, but participants enrolled on the trial continued to be followed up according to the protocol. A close-down plan was formed and implemented.

Lessons learnt from early closure

The challenge faced by many trials that closed early during the pandemic was slow recruitment of the target population. The authors considered several adjustments to the trial and increased the flexibility of the protocol. For any future trials in this area, we would increase the adaptive elements of the design to enable more of the study to be salvaged under similar circumstances. We learnt that remote methods of follow-up are generally acceptable to participants and site staff. We also explored remote monitoring and possibilities for central follow-up. Flexibility and responsiveness of sponsors and regulators during this time enabled useable data to be gathered from those enrolled in the trial at the time of closure, and careful financial stewardship by the study team enabled full close out to proceed.

Understanding new ways of working

We surveyed all CHAPS sites to explore their interest in taking part in a potentially remodelled version of the trial in the future and to examine feasibility, considering the ongoing capacity issues within the NHS post pandemic. Seventy-seven per cent of sites felt that the CHAPS research question was still important, and 73% expressed interest in recruiting to a remodelled trial if this was ever funded. We also asked:

Do you think remote follow-up would aid recruitment or capacity issues?

Ninety-seven per cent answered 'yes'. Post-COVID, capacity within the NHS is a major issue and easing the

burden of follow-up on local staff would enable research centres to focus on recruitment. Follow-up in the form of video calls and photographic assessment could facilitate trial delivery and could also facilitate observer-blinding. It would also enable patients to take part who were previously excluded from trials due to work/home commitments, or difficulty in travel. A surge in the use of digital technologies was seen during the pandemic. An Ofcom survey showed that in 2019, 55% of people aged > 55 years owned a smartphone, a figure that rose to 83% in 2021.²²

The authors would also advise removing elements of the trial design that sites found burdensome, in line with guidance from the recently published Government white paper 'The Future of UK Clinical Research Delivery: 2021 to 2022 Implementation Plan'. In CHAPS, for instance, we would remove certain questionnaires as well as the planned process evaluation to ease recruitment and streamline the overall design. The paper also supports innovative models of trial delivery, including hub and spoke models and remote participation.

Patient and public involvement

People with lived experience of DVT were invited to act as lay representatives for the study. Their role was to act as a voice for participants and patients with DVT and PTS throughout the course of the study and to ensure that patients' interests were at the fore when decisions about the trial were made. They were actively involved in the design of the research, the management of the research and the development of participant information resources.

A short biography on each patient and public involvement (PPI) representative was incorporated into study newsletters to inform the local sites of their involvement. This also enabled the PPI representatives to feel integrated into the research team. The Trial Manager met regularly with each representative to discuss any points raised during the Trial Steering Committee meetings and to discuss implications of any study amendments throughout the trial. The representatives also regularly e-mailed their helpful thoughts and advice to the Trial Manager who fed back to the study team.

After the closure of CHAPS, The Trial Manager e-mailed each PPI representative a series of short questions to ask them about their experience working on the trial. Their answers are illustrated here:

1. *How did you find working as a patient representative on the CHAPS study?*

I enjoyed being involved and learned a lot about how patient trials and the NICR operates. The outcome was frustrating, but given the issues with the pandemic, I was amazed at the level of support you managed to get from the hospitals.

2. *Was there anything you think could be improved for patient representatives who may take part in a similar study?*

No.

3. *Was there anything you thought was particularly good about working on CHAPS?*

Being on the steering committee meant that I could follow the trial outcome a lot better than before, where I had no significant involvement after the trial started.
Patient representative

4. *Did you feel your opinions and voice was heard by the CHAPS team members?*

Yes, but I did not feel I had a lot to offer.

5. *Do you have anything else you think that the study team should take into consideration next time they involve lay patient representatives?*

For representatives who are only involved before the trial gets underway, maybe some form of regular communication on how the trial is progressing, if this is not done already.

Thrombosis UK was involved in the grant development stage of the project, and a representative supported the project throughout. Their involvement was crucial in providing a lay perspective on patient and public perceptions of the study, and they offered key advice on recovery strategies during the pandemic.

Dissemination

Dissemination to the scientific community will be a formal presentation by the Chief Investigator at the UK Vascular Society and the International Union of Phlebology conferences. The Trial Manager will present results at the Thrombosis UK conference. A scientific manuscript has been published in a scientific journal detailing the trial results, reasons for early termination and implication for future research in the field.¹⁸

The CHAPS team will disseminate the results of the study to patients via the trial website. Links to the web page will be made available to each recruiting trust to

aid dissemination to the public via their Twitter (Twitter, Inc., San Francisco, CA, USA) and social media channels. PTS remains a huge problem for many patients post DVT, and as such, we will continue to garner their views as to whether they think this research is useful and how it could be adapted in the future via short surveys and PPI work. Our PPI representatives have agreed to continue working with the team on related research.

Equality, diversity and inclusion

The CHAPS enrolled 152 participants from 24 secondary care centres in England. A total of 68% of participants were male and 32% were female. Minoritised ethnic groups accounted for 30% of enrolled participants, and 82% defined themselves as White (inclusive of White British and White other, e.g. Irish, Gypsy or Irish traveller). This is in line with the 2021 UK national census, where 82% of residents in England and Wales identified their ethnic group within the high-level 'White' category.²³

Impact and learning

The barriers described in this synopsis together prevented sites being able to recruit the required sample size and led to its early termination. Nevertheless, the efforts involved in setting up, troubleshooting and adapting this study resulted in some key achievements. Firstly, the study team has established a strong network of investigators across the UK and overseas who are willing to collaborate in future studies of PTS. Secondly, procurement of stockings for the trial through NHS supply chains slowed down site set-up. To adhere to the project management plan, the co-ordinating centre switched stocking supplier to Medi UK, enhancing the deliverability of the trial. Standardising the intervention through provision of robust training to local research teams in measuring and fitting stockings may have potentially improved adherence. The lessons learnt from CHAPS are also easily applicable to other RCTs in compression therapy.

Research recommendations

We have identified the following for future research in this area:

- repeat the trial with a streamlined design that would also ensure sufficient recruitment and statistical power
- explore mechanisms to increase the adherence of stockings for patients post DVT

- perform a full health economic analysis to examine the cost of supplying stockings to this population.

Conclusions

Despite the original hypothesis of the CHAPS trial, that GCS may reduce the incidence of PTS in adults with first DVT, the number of participants recruited was not sufficient to yield any meaningful results. The findings suggest that there was less PTS in the intervention arm, and these data may be useful in informing future studies.

The CHAPS underlines the importance of clinical trials that investigate optimal strategies to prevent the PTS. The study also highlights the need for adaptive trial designs and demonstrates the acceptability of remote and centralised follow-up.

Additional information

CRedit contribution statement

Ankur Thapar (<https://orcid.org/0000-0003-4542-1100>): Conceptualisation (equal), Methodology (equal), Investigation (equal), Funding acquisition (equal), Writing – reviewing and editing (equal).

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Nicky Cullum: Conceptualisation (equal).

David Epstein: Conceptualisation (equal).

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Robert Horne: Conceptualisation (equal).

Joseph Shalhoub: Conceptualisation (equal).

Annya Stephens-Boal: PPI contributions.

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Trial Management Group

The Trial Management Group comprised Professor Alun Davies (as chief investigator), Mr Ankur Thapar (as coinvestigator), Ms Rebecca Lawton (as Trial Manager), Ms Sarrah Peerbux (as Trial Manager), Mr Imad Adamestam (as statistician), Anny Briola (as statistician), Agnes Tello (as Senior Research Manager) and Professor John Norrie (as senior statistician).

Edinburgh Clinical Trials Unit

The following members were part of the Edinburgh Clinical Trials Unit study team: Michelle Stevens (Data Manager).

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Trial Steering Committee

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All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Ethics statement

The National Research Ethics Service (NRES) granted ethical approval from London Bloomsbury Research Ethics Committee (Reference 19/LO/1585) on 14th October 2019.

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Rebecca Lawton, Sarrah Peerbux and Imad Adamestam have no competing interests to declare.

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Trial registration

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Award publications

This synopsis provided an overview of the research award CHAPS: *Compression Hosiery to Avoid Post-Thrombotic Syndrome*.

Other articles published as part of this thread are:

Lawton R, Hunt BJ, Norrie J, Shalhoub J, Thapar A, Davies AH. Compression hosiery to avoid post-thrombotic syndrome (CHAPS) trial. *Eur J Vasc Endovasc Surg* 2022;**64**:431–2. <https://doi.org/10.1016/j.ejvs.2022.07.056>

Thapar A, Lawton R, Bradbury A, Cullum N, Gohel M, Horne R, et al. Compression hosiery to avoid post-thrombotic syndrome: CHAPS randomized clinical trial. *Br J Surg* 2025;**112**:znaf018. <https://doi.org/10.1093/bjs/znaf018>

For more information about this research, please view the award page (www.fundingawards.nihr.ac.uk/award/17/147/47).

Additional outputs

Thapar A, Lawton R, Burgess L, Shalhoub J, Bradbury A, Cullum N, et al. Compression hosiery to avoid post-thrombotic syndrome (CHAPS) protocol for a randomised controlled trial [ISRCTN73041168]. *BMJ Open* 2021;**11**:e044285. <https://doi.org/10.1136/bmjopen-2020-044285>

Conference abstracts or presentations

Compression Hosiery to prevent Post Thrombotic Syndrome Presentation for Thrombosis UK Webinar Series.

Update on Compression Hosiery to Prevent Post Thrombotic Syndrome Presentation for the Lets Talk Clots Virtual Conference to Provide an Update on CHAPS.

Compression Hosiery to Prevent Post Thrombotic Syndrome 17th Annual Conference of Venous Association of India.

Compression Hosiery to Prevent Post Thrombotic Syndrome VSGBI Conference Results Presentation.

Compression Hosiery to Prevent Post Thrombotic Syndrome VEITH Symposium.

Other

Research Stand at the Vascular Society. Attendance at the Vascular Society to Promote CHAPS amongst Potential Principal Investigators.

Throughout the study

Twitter – Updating the Twitter feed with updates/progress re recruitment/site set-up.

About this synopsis

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List of abbreviations

BMI	body mass index
CHAPS	Compression Hosiery to Avoid Post-Thrombotic Syndrome
DVT	deep vein thrombosis/deep venous thrombosis
GCS	graduated compression stockings
NIHR	National Institute for Health and Care Research
NNT	number needed to treat
PPI	patient and public involvement
PTS	post-thrombotic syndrome
RCT	randomised controlled trial
SAP	statistical analysis plan

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Appendix 1 Compression Hosiery to Avoid Post-Thrombotic Syndrome flow diagram

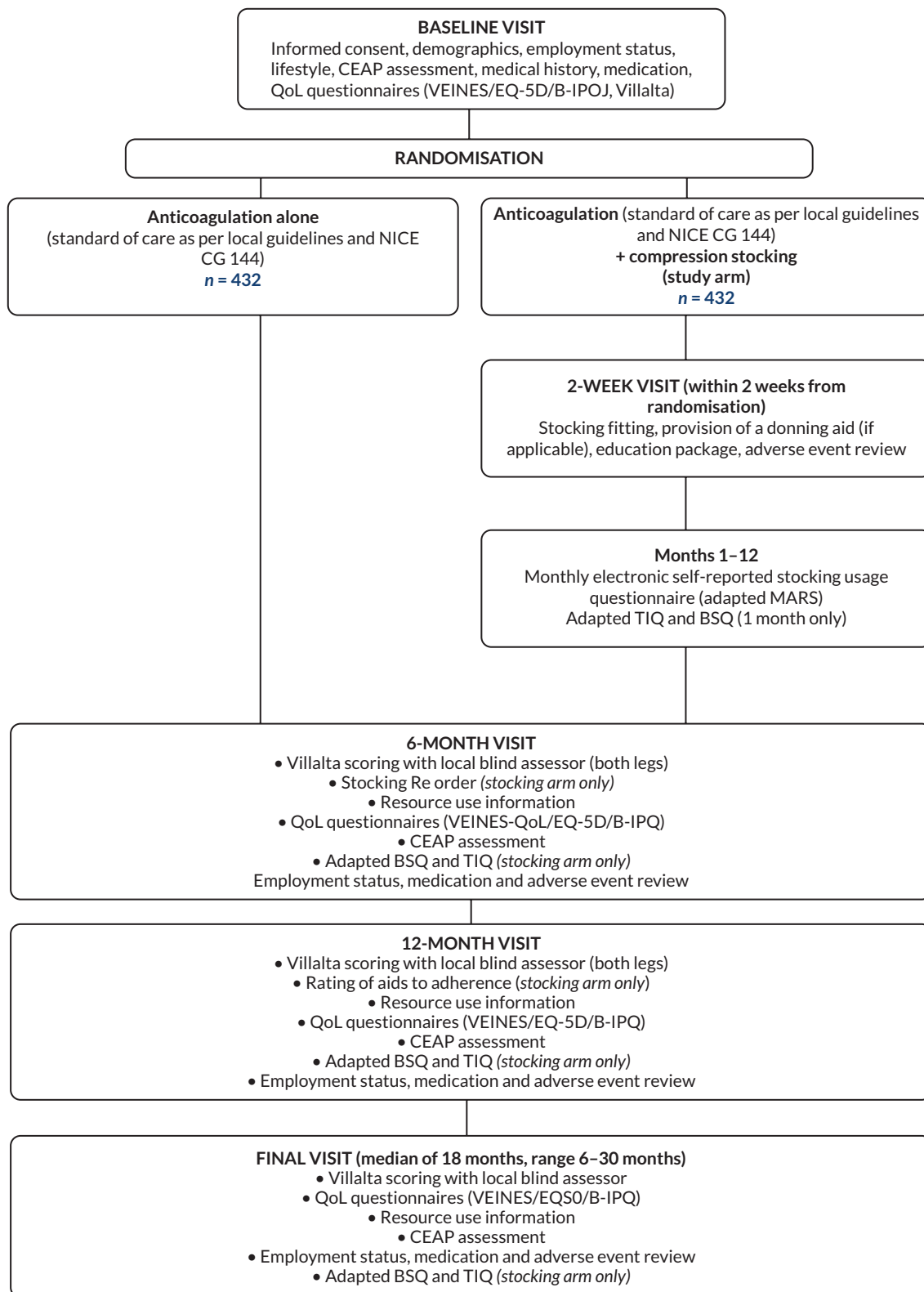


FIGURE 1 The CHAPS flow diagram. BSQ, Beliefs about Stockings Questionnaire; CEAP, Comprehensive Classification System for Chronic Venous Disorders; EQ-5D, EuroQol-5 Dimensions; QoL, quality of life; TIQ, Treatment Intrusiveness Questionnaire.

