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[Intervention Review]

Graduated compression stockings for prevention of deep vein thrombosis

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ABSTRACT

Background

Hospitalised patients are at increased risk of developing deep vein thrombosis (DVT) in the lower limb and pelvic veins, on a background of prolonged immobilisation associated with their medical or surgical illness. Patients with DVT are at increased risk of developing a pulmonary embolism (PE). The use of graduated compression stockings (GCS) in hospitalised patients has been proposed to decrease the risk of DVT. This is an update of a Cochrane Review first published in 2000, and last updated in 2014.

Objectives

To evaluate the effectiveness and safety of graduated compression stockings in preventing deep vein thrombosis in various groups of hospitalised patients.

Search methods

For this review the Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), and trials registries on 21 March 2017; and the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE Ovid, Embase Ovid, CINAHL Ebsco, AMED Ovid, and trials registries on 12 June 2018.

Selection criteria

Randomised controlled trials (RCTs) involving GCS alone, or GCS used on a background of any other DVT prophylactic method. We combined results from both of these groups of trials.

Data collection and analysis

Two review authors (AS, MD) assessed potentially eligible trials for inclusion. One review author (AS) extracted the data, which a second review author (MD) cross-checked and authenticated. Two review authors (AS, MD) assessed the methodological quality of trials with the Cochrane 'Risk of bias' tool. Any disagreements were resolved by discussion with the senior review author (TL). For dichotomous outcomes, we calculated the Peto odds ratio and corresponding 95% confidence interval. We pooled data using a fixed-effect model. We used the GRADE system to evaluate the overall quality of the evidence supporting the outcomes assessed in this review.

Main results

We included 20 RCTs involving a total of 1681 individual participants and 1172 individual legs (2853 analytic units). Of these 20 trials, 10 included patients undergoing general surgery; six included patients undergoing orthopaedic surgery; three individual trials included patients undergoing neurosurgery, cardiac surgery, and gynaecological surgery, respectively; and only one trial included medical patients. Graduated compression stockings were applied on the day before surgery or on the day of surgery and were worn up until discharge or until

the participants were fully mobile. In the majority of the included studies DVT was identified by the radioactive 125 uptake test. Duration of follow-up ranged from seven to 14 days. The included studies were at an overall low risk of bias.

We were able to pool the data from 20 studies reporting the incidence of DVT. In the GCS group, 134 of 1445 units developed DVT (9%) in comparison to the control group (without GCS), in which 290 of 1408 units developed DVT (21%). The Peto odds ratio (OR) was 0.35 (95% confidence interval (CI) 0.28 to 0.43; 20 studies; 2853 units; high-quality evidence), showing an overall effect favouring treatment with GCS ($P < 0.001$).

Based on results from eight included studies, the incidence of proximal DVT was 7 of 517 (1%) units in the GCS group and 28 of 518 (5%) units in the control group. The Peto OR was 0.26 (95% CI 0.13 to 0.53; 8 studies; 1035 units; moderate-quality evidence) with an overall effect favouring treatment with GCS ($P < 0.001$). Combining results from five studies, all based on surgical patients, the incidence of PE was 5 of 283 (2%) participants in the GCS group and 14 of 286 (5%) in the control group. The Peto OR was 0.38 (95% CI 0.15 to 0.96; 5 studies; 569 participants; low-quality evidence) with an overall effect favouring treatment with GCS ($P = 0.04$). We downgraded the quality of the evidence for proximal DVT and PE due to low event rate (imprecision) and lack of routine screening for PE (inconsistency).

We carried out subgroup analysis by speciality (surgical or medical patients). Combining results from 19 trials focusing on surgical patients, 134 of 1365 (9.8%) units developed DVT in the GCS group compared to 282 of 1328 (21.2%) units in the control group. The Peto OR was 0.35 (95% CI 0.28 to 0.44; high-quality evidence), with an overall effect favouring treatment with GCS ($P < 0.001$). Based on results from seven included studies, the incidence of proximal DVT was 7 of 437 units (1.6%) in the GCS group and 28 of 438 (6.4%) in the control group. The Peto OR was 0.26 (95% CI 0.13 to 0.53; 875 units; moderate-quality evidence) with an overall effect favouring treatment with GCS ($P < 0.001$). We downgraded the evidence for proximal DVT due to low event rate (imprecision).

Based on the results from one trial focusing on medical patients admitted following acute myocardial infarction, 0 of 80 (0%) legs developed DVT in the GCS group and 8 of 80 (10%) legs developed DVT in the control group. The Peto OR was 0.12 (95% CI 0.03 to 0.51; low-quality evidence) with an overall effect favouring treatment with GCS ($P = 0.004$). None of the medical patients in either group developed a proximal DVT, and the incidence of PE was not reported.

Limited data were available to accurately assess the incidence of adverse effects and complications with the use of GCS as these were not routinely quantitatively reported in the included studies.

Authors' conclusions

There is high-quality evidence that GCS are effective in reducing the risk of DVT in hospitalised patients who have undergone general and orthopaedic surgery, with or without other methods of background thromboprophylaxis, where clinically appropriate. There is moderate-quality evidence that GCS probably reduce the risk of proximal DVT, and low-quality evidence that GCS may reduce the risk of PE. However, there remains a paucity of evidence to assess the effectiveness of GCS in diminishing the risk of DVT in medical patients.

PLAIN LANGUAGE SUMMARY

Graduated compression stockings for prevention of deep vein thrombosis during a hospital stay

Background

Deep vein thrombosis (DVT) is a blood clot that forms in a vein deep in the body, usually in the leg or pelvic veins. A number of factors such as reduced mobility, older age, obesity, active cancer, major surgery, major injuries, history of previous DVT, family history of DVT, and recent period of illness may increase the risk of developing a DVT. Hospital patients, who often have one or more of these risk factors, are at particular risk of developing DVT, either immediately after surgery or if they are immobile due to a medical illness.

Symptoms of DVT vary from none to pain and swelling in the legs. A blood clot can move from the leg to the lungs, with the danger of pulmonary embolism (PE) and death. The main treatment for DVT includes the use of blood-thinning drugs (anticoagulation). Deep vein thrombosis usually resolves, but it can have long-term effects such as high venous pressure in the leg, leg pain, swelling, darkening of the skin, and inflammation.

Deep vein thrombosis can be prevented with the use of compression or drugs. Drugs can cause bleeding, which is a particular concern in surgical patients. Graduated compression stockings (GCS) help prevent the formation of blood clots in the legs by applying varying amounts of pressure to different parts of the leg.

Study characteristics and key results

We identified 20 randomised controlled trials (studies in which participants are assigned to a treatment group using a random method) (2853 analytic units consisting of 1681 individual patients and 1172 individual legs) in our most recent search on 12 June 2018. Nine trials compared wearing stockings to no stockings, and 11 compared stockings plus another method with that method alone. The other methods used were dextran 70, aspirin, heparin, and mechanical sequential compression. Of the 20 trials, 10 included patients undergoing general surgery; six included patients undergoing orthopaedic surgery; three individual trials included patients undergoing neurosurgery, cardiac surgery, and gynaecological surgery, respectively; and only one trial included medical patients (patients who were admitted to the hospital

for reasons other than surgery). The compression stockings were applied on the day before surgery or on the day of surgery and were worn up until discharge or until the patients were fully mobile. Thigh-length stockings were used in the vast majority of included studies. The included studies were of good quality overall. We found that wearing GCS reduced the overall risk of developing DVT, and probably also DVT in the thighs. We found that GCS may also reduce the risk of PE amongst patients undergoing surgery. As only one trial included medical patients, results for this population are limited. The occurrence of problems associated with wearing GCS was poorly reported in the included studies.

Quality of the evidence

Our review confirmed that GCS are effective in reducing the risk of DVT in hospitalised surgical patients (high-quality evidence). It also demonstrated that GCS probably reduce the risk of developing DVT in the thighs (proximal DVT, moderate-quality evidence) and PE (low-quality evidence). Reasons for downgrading the quality of the evidence included low event rate (i.e. small number of participants who developed DVT) and uncertainty due to only a small number of patients being routinely screened for proximal DVT or PE. Limited evidence was available for hospitalised medical patients, with only one study suggesting that GCS may prevent DVT in such patients.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Graduated compression stockings for prevention of deep vein thrombosis - all patients

Graduated compression stockings for prevention of deep vein thrombosis

Patient or population: Hospitalised patients¹

Setting: Inpatients

Intervention: GCS

Comparison: No GCS

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of units/ participants ² (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no GCS	Risk with GCS				
Deep vein thrombosis (DVT) Follow-up: 7 to 14 days, or until discharge	Study population		OR 0.35 (0.28 to 0.43)	2853 (20 RCTs)	⊕⊕⊕⊕ HIGH	Graduated compression stockings reduce the incidence of DVT in hospitalised patients. However, studies did not routinely distinguish between symptomatic and asymptomatic DVTs.
	206 per 1000	83 per 1000 (68 to 100)				
Proximal DVT Follow-up: 7 to 14 days, or until discharge	Study population		OR 0.26 (0.13 to 0.53)	1035 (8 RCTs)	⊕⊕⊕⊖ MODERATE ³	Graduated compression stockings probably reduce the incidence of proximal DVT in hospitalised patients. There was a relatively low event rate overall, and studies did not routinely distinguish between symptomatic and asymptomatic proximal DVTs.
	54 per 1000	15 per 1000 (7 to 29)				
Pulmonary embolism Follow-up: 7 to 30 days	Study population		OR 0.38 (0.15 to 0.96)	569 (5 RCTs)	⊕⊕⊖⊖ LOW ⁴	Graduated compression stockings may slightly reduce the incidence of pulmonary embolism in hospitalised patients. Pulmonary embolism was not routinely assessed in most included studies, and the overall event rate was very low.
	49 per 1000	19 per 1000 (8 to 47)				
Adverse effects and complications Follow-up: until discharge	See comment		-	-	-	Some participants removed stockings due to discomfort or poor fitting, however adverse effects and complications were not routinely reported quantitatively in the included studies.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **DVT:** deep vein thrombosis; **GCS:** graduated compression stockings; **OR:** odds ratio; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

¹Included patients admitted for surgical procedures (including abdominal, orthopaedic, neurosurgical, gynaecological surgery) and medical illness (acute myocardial infarction).

²Numbers refer to number of analytic units (either individual legs or individual participants).

³We downgraded the quality of the evidence by one step due to the low event rate in the GCS group (imprecision).

⁴We downgraded the quality of the evidence by two steps as routine screening for pulmonary embolism was done in only two of the five RCTs, and the CIs were wide (inconsistency).

Summary of findings 2. Graduated compression stockings for prevention of deep vein thrombosis in surgical patients

Graduated compression stockings for prevention of deep vein thrombosis

Patient or population: Patients hospitalised for surgical procedures¹

Setting: Inpatients

Intervention: GCS

Comparison: No GCS

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of units/ participants ² (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no GCS	Risk with GCS				
Deep vein thrombosis (DVT) Follow-up: 7 to 14 days, or until discharge	Study population		OR 0.35	2693	⊕⊕⊕⊕ HIGH	Graduated compression stockings reduce the incidence of DVT in hospitalised surgical patients. However, studies did not routinely distinguish between symptomatic and asymptomatic DVTs.
	212 per 1000	86 per 1000 (70 to 106)	(0.28 to 0.44)	(19 RCTs)		
Proximal DVT	Study population		OR 0.26	875	⊕⊕⊕⊖ MODERATE ³	Graduated compression stockings probably reduce the incidence of proximal DVT in hospitalised surgical patients. However, studies did not routinely dis-
	64 per 1000	17 per 1000	(0.13 to 0.53)	(7 RCTs)		

Follow-up: 7 to 14 days, or until discharge	(9 to 35)					tinguish between symptomatic and asymptomatic proximal DVTs. There was a relatively low event rate overall.
Pulmonary embolism	Study population		OR 0.38	569	⊕⊕⊕⊕ LOW ⁴	Graduated compression stockings may slightly reduce the incidence of pulmonary embolism in hospitalised surgical patients. However, pulmonary embolism was not routinely assessed in most included studies, and the overall event rate was very low.
Follow-up: 7 to 30 days, or until discharge	49 per 1000	19 per 1000 (8 to 47)	(0.15 to 0.96)	(5 RCTs)		
Adverse effects and complications	See comment		-	-	-	Some participants removed stockings due to discomfort or poor fitting, however adverse effects and complications associated with wearing GCS were not routinely reported quantitatively in the included studies.
Follow-up: until discharge						

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **DVT:** deep vein thrombosis; **GCS:** graduated compression stockings; **OR:** odds ratio; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

¹Included patients admitted for surgical procedures (including abdominal, orthopaedic, neurosurgical, gynaecological surgery).

²Numbers refer to number of analytic units (either individual legs or individual participants).

³We downgraded the quality of the evidence by one step due to the low event rate in the GCS group (imprecision).

⁴We downgraded the quality of the evidence by two steps as routine screening for pulmonary embolism was done in only two of the five RCTs, and the CIs were wide (inconsistency).

Summary of findings 3. Graduated compression stockings for prevention of deep vein thrombosis in medical patients

Graduated compression stockings for prevention of deep vein thrombosis

Patient or population: Patients hospitalised following acute myocardial infarction

Setting: Inpatients

Intervention: GCS

Comparison: No GCS

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of units (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no GCS	Risk with GCS				
Deep vein thrombosis (DVT) Follow-up: 8 days or discharge or until development of DVT	Study population		OR 0.12 (0.03 to 0.51)	160 (1 RCT)	⊕⊕⊕⊕ LOW ¹	Graduated compression stockings may reduce incidence of DVT in hospitalised medical patients. However, results are based on a single study on medical patients hospitalised following acute myocardial infarction (Kierkegaard 1993).
	100 per 1000	13 per 1000 (3 to 54)				
Proximal DVT Follow-up: 8 days or discharge or until development of DVT	Study population		Not estimable	160 (1 RCT)	-	None of the participants in either group of this single RCT with a small sample size developed proximal DVT.
	0 per 1000	0 per 1000 (0 to 0)				
Pulmonary embolism	See comment		-	-	-	No studies reported on this outcome. There is paucity of evidence to evaluate the effect of GCS on reducing incidence of pulmonary embolism in hospitalised medical patients.
Adverse effects and complications	See comment		-	160 (1 RCT)	-	There are rare reports of post-thrombotic changes in participants who developed DVT in the single included RCT.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **DVT:** deep vein thrombosis; **GCS:** graduated compression stockings; **OR:** odds ratio; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

¹We downgraded the quality of the evidence by two steps as there was only one study and a low event rate in the GCS group (imprecision).

BACKGROUND

Description of the condition

The occurrence of one or more factors of Virchow's triad (stasis of blood, endothelial injury, and hypercoagulability of blood) in the venous system often leads to deep vein thrombosis (DVT) (Virchow 1858). Diagnosis of DVT is difficult as the patient history is not specific, and symptoms vary from no symptoms to pain and swelling in the legs. The sequelae of DVT vary from complete resolution of the clot without any ill effects through to death due to pulmonary embolism (PE).

Risk factors associated with the development of DVT include age over 60 years, active cancer, obesity, major surgery, major trauma, prolonged immobilisation, pregnancy, history of thromboembolic disease, and acute medical illness. Thromboembolic risk factors are particularly common amongst hospitalised patients, with baseline incidence of DVT in 29% of surgical patients and 24% in medical patients, and incidence of symptomatic PE of 3% and 1%, respectively, without the use of thromboprophylaxis (NICE 2010).

Morbidity due to DVT includes post-thrombotic syndrome (PTS), which encompasses chronic venous hypertension causing limb pain, swelling, hyperpigmentation (darkening of the skin), dermatitis (inflammation of the skin), ulcers, and lipodermatosclerosis (a hardening of the skin that may gain a red or brown pigmentation and is accompanied by wasting of the subcutaneous fat). Data from a prospective multicentre cohort study found that 43% of patients with symptomatic DVT developed features of PTS at two-year follow-up (Kahn 2008).

Mortality associated with DVT is greatest in the first 30 days, at 3% to 6%, though the risk of death remains increased even at long-term follow-up (Søgaard 2014). Various reports suggest that 28% to 41% of patients with DVT subsequently develop a PE, which is associated with an increase in risk of 30-day mortality to approximately 12% (White 2003).

Patients who are at risk of developing DVT are categorised into three groups of low, moderate, and high risk according to the International Consensus Statement and Thromboembolic Risk Factor (THRIFT) consensus group guidelines (ICS 2013; THRIFT 1992). However, guidelines on prophylaxis of venous thromboembolism from the National Institute for Health and Care Excellence and the Scottish Intercollegiate Guidelines Network no longer categorise patients into low-, moderate-, and high-risk groups (NICE 2010; SIGN 2010), instead looking at risk factors for developing DVT in hospitalised patients on an individual basis.

Description of the intervention

Both mechanical and pharmacological methods are used in the prevention of DVT. Pharmacological methods alter the blood coagulation profile; the major disadvantage of this is the risk of bleeding, which may be of particular concern in surgical patients. For example, the altered coagulation may lead to joint haematomas following joint replacement surgery and intracranial haemorrhage following head injury or neurosurgery. Mechanical methods include techniques such as intermittent pneumatic compression (IPC) and wearing of graduated compression stockings (GCS).

How the intervention might work

The exact mechanism by which GCS function is unknown. However, there is evidence to suggest that they exert graded circumferential pressure distally to proximally and, when combined with muscular activity in the limb, are thought to displace blood from the superficial to the deep venous system via the perforating veins. It is argued that this effectively increases the velocity and volume of flow in the deep system thereby potentially preventing thrombosis (Benko 2001).

Why it is important to do this review

Despite the theoretical effectiveness and widespread use of compression stockings, their clinical effectiveness needs further appraisal. Improper application of stockings may potentially cause complications such as discomfort, oedema of the legs, DVT, and arterial ischaemia. Stockings may also be contraindicated for medical reasons. The extent to which the leg profile of patients may limit effectiveness has not been addressed. This review did not address the recommendations regarding the ideal length of stockings (knee length versus thigh length), which are assessed by a separate Cochrane Review (Sajid 2012).

The use of GCS amongst surgical patients is estimated to cost the National Health Service (NHS) GBP 63.1 million annually (GAPS). A strong evidence base is therefore needed to justify the routine use of GCS amongst hospitalised patients.

OBJECTIVES

To evaluate the effectiveness and safety of graduated compression stockings in preventing deep vein thrombosis in various groups of hospitalised patients.

We tested the following hypotheses:

- compression stockings are effective in preventing DVT in hospitalised patients (excluding stroke);
- in all moderate-risk patients, compression stockings alone are adequate for DVT prophylaxis, except for patients for whom stockings are specifically contraindicated;
- stockings are unnecessary in low-risk patients;
- complications are associated with the use of compression stockings.

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomised controlled trials (RCTs) that involved the use of compression stockings for DVT prophylaxis.

Types of participants

We included patients of either sex and any age hospitalised for conditions other than stroke.

Types of interventions

We included trials in which the use of graduated compression stockings (GCS) was compared with no prophylaxis, and those studies in which the use of GCS was compared with no stockings on a background of another method of DVT prophylaxis in both the

treatment and control group (e.g. aspirin, heparin). We analysed both groups of trials together in this update as they both assessed the same treatment effect (i.e. GCS versus no GCS).

Types of outcome measures

Primary outcomes

- Diagnosis of DVT, either all DVT or proximal DVT, identified by ultrasound, venogram, or isotope studies

Secondary outcomes

- Diagnosis of PE, identified by a ventilation perfusion lung scan, pulmonary angiogram, or postmortem examination
- Complications and adverse effects arising from the use of GCS

Search methods for identification of studies

We placed no restrictions on language or publication status.

Electronic searches

For this update, the Cochrane Vascular Information Specialist (CIS) searched the following databases for relevant trials:

- the Cochrane Vascular Specialised Register (21 March 2017);
- the Cochrane Central Register of Controlled Trials (CENTRAL (2017, Issue 2)) via the Cochrane Register of Studies Online (21 March 2017).

See [Appendix 1](#) for details of the search strategy used to search CENTRAL.

The Cochrane Vascular Specialised Register is maintained by the CIS and is constructed from weekly electronic searches of MEDLINE Ovid, Embase Ovid, CINAHL Ebsco (Cumulative Index to Nursing and Allied Health Literature), AMED Ovid (Allied and Complementary Medicine), and through handsearching relevant journals.

The CIS also searched the following trial registries for details of ongoing and unpublished studies (21 March 2017):

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov);
- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (www.who.int/trialsearch);
- ISRCTN register (www.isrctn.com/).

See [Appendix 2](#) for details of the search strategies used.

The CIS subsequently performed a top-up search on 12 June 2018, searching the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE Ovid (2017 and 2018 only), Embase Ovid (2017 and 2018 only), CINAHL Ebsco (2017 and 2018 only), AMED Ovid (2017 and 2018 only), and the trials registries ClinicalTrials.gov and WHO ICTRP. See [Appendix 3](#) for details of the search strategies.

Searching other resources

We searched the reference lists of all potentially eligible studies identified from the electronic searches to find additional trials.

Data collection and analysis

Selection of studies

We have specified the criteria for the selection of trials above. Two review authors (AS, MD) carried out the selection of trials for inclusion in this update, which the senior review author (TL) checked and approved.

One review author (AS) carried out the initial screening of all retrieved studies based on titles and abstracts in order to identify obvious exclusions (i.e. studies not relevant to the review). Where there was uncertainty regarding the relevance of a particular study, a second review author (MD) was consulted. Two review authors (AS, MD) independently assessed the remaining records so as to avoid exclusion of any relevant articles. Next, full papers were extracted for the remaining articles, which two review authors (AS, MD) independently assessed for inclusion (see [Criteria for considering studies for this review](#)). In case of disagreement between review authors, consensus was reached by discussion with a third review author (TL). Finally, all eligible, relevant studies based on the abovementioned criteria were included in the review.

Data extraction and management

For this update, one review author (AS) performed data extraction and entered data onto a data extraction form. Another review author (MD) then cross-checked the data. We extracted the following information.

- Age
- Sex
- DVT risk groups to which participants belonged
- Duration of application of stockings
- Types and length of stockings
- Incidence of DVT
- PE
- Adverse effects
- Investigations used to make the diagnoses

Assessment of risk of bias in included studies

Two review authors (AS, MD) independently assessed the risk of bias for all the included studies based on six domains: random sequence generation, allocation concealment, blinding (participant and assessor), incomplete outcome data, selective reporting, and other biases. We used the 'Risk of bias' assessment tool outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* to determine whether studies were free of potential bias, assessing studies as at low risk, high risk, or unclear risk of bias if the available information was inadequate ([Higgins 2011](#)). Any discrepancies in opinion were discussed and consensus reached. Blinding of participants to their treatment group (i.e. whether they wore GCS or not) was inherently difficult, therefore blinding of assessors to treatment groups was deemed the most appropriate method to minimise risk of bias.

Measures of treatment effect

The effectiveness of treatment (i.e. the use of GCS) was assessed by recording the incidence of DVT in the treatment (stockinged) group compared to that in the control (non-stockinged) group. Deep vein thrombosis was diagnosed using an objective method of

assessment such as ultrasound, venogram, or isotope studies. We did not combine individual patient data from different trials.

We performed analysis of the cumulative data using Peto's odds ratio (OR) with 95% confidence interval (CI) employing a fixed-effect model. We used fixed-effect analysis since the vast majority of included studies were based on surgical patients at medium or high risk of developing DVT. Furthermore, we also considered that fixed-effect analysis would help minimise bias due to the low event rate amongst a number of included studies with a small sample size. We used Review Manager 5, the statistical package provided by Cochrane, for cumulative analysis of the included trials ([RevMan 2012](#)).

Unit of analysis issues

Individual patients were the analytic units except in seven trials ([Bergqvist 1984](#); [Kierkegaard 1993](#); [Mellbring 1986](#); [Scurr 1977](#); [Scurr 1987](#); [Shirai 1985](#); [Torngren 1980](#)), where one limb was randomised to act as control and the other was treated.

Since a thrombus can embolise from either the control or stockinged leg, trials randomising individual legs could not be used to compare the incidence of PE, therefore where data were available, individual patients were used as the unit of analysis for comparing incidence of PE.

Dealing with missing data

Complete primary outcome data were available for participants excluded postrandomisation in only four trials ([Allan 1983](#); [Scurr 1977](#); [Torngren 1980](#); [Wille-Jorgensen 1991](#)). Participants had been excluded postrandomisation in an additional eight trials ([Bergqvist 1984](#); [Fredin 1989](#); [Holford 1976](#); [Hui 1996](#); [Kalodiki 1996](#); [Mellbring 1986](#); [Ohlund 1983](#); [Wille-Jorgensen 1985](#)), though the confirmation of the presence or absence of DVT amongst these excluded participants was not reported. We were unable to assess [Shirai 1985](#) for missing data, as it was only published in Japanese. There were no reported exclusions postrandomisation in the remaining seven trials ([Barnes 1978](#); [Chin 2009](#); [Kierkegaard 1993](#); [Scurr 1987](#); [Tsapogas 1971](#); [Turner 1984](#); [Turpie 1989](#)). Due to the small number of trials reporting outcome data for participants excluded postrandomisation, we performed a per-protocol analysis.

Similarly, complete outcome data were unavailable for secondary outcomes, therefore we performed a per-protocol analysis.

Assessment of heterogeneity

We used the I^2 statistic to quantify heterogeneity. We considered heterogeneity to be statistically significant for a $P < 0.1$.

Assessment of reporting biases

We assessed reporting bias by visual inspection of funnel plots.

Data synthesis

In previous versions of this review, we performed data synthesis based on two groups as follows.

- Group 1: GCS only in the treatment group and no prophylaxis in the control group.
- Group 2: GCS in the treatment group and another method of DVT prophylaxis in both the treatment and control groups.

Since both of these groups test the same treatment effect (i.e. with stockings versus without stockings), we merged all trials in the 2014 update to increase the power of the review.

We tested comparisons of results using a fixed-effect model for the meta-analysis.

Subgroup analysis and investigation of heterogeneity

We subgrouped trials based on the speciality under which the participant had been hospitalised. Most participants underwent either general surgical or orthopaedic surgical procedures. We undertook subgroup analyses in Review Manager 5 using the method described by [Deeks 2001](#).

Sensitivity analysis

We performed sensitivity analyses to assess the effect of the following three potential areas of bias on the robustness of decisions made during the review process.

- Method of randomisation: trials reporting use of an appropriate method of randomisation versus use of an unclear method of randomisation.
- Unit of analysis of randomisation: individual legs versus individual participants.
- Use of a background method of thromboprophylaxis.
- Method of diagnosis of DVT.

'Summary of findings' table

We presented the main findings of this update in 'Summary of findings' tables. We considered the quality of evidence, magnitude of effect of interventions examined, and the sum of available data for all outcomes of this review (DVT, proximal DVT, PE, adverse events and complications). We presented the findings for all patients ([Summary of findings for the main comparison](#)), surgical patients ([Summary of findings 2](#)), and medical patients ([Summary of findings 3](#)) according to GRADE principles, as described by [Higgins 2011](#) and [Atkins 2004](#). We evaluated evidence on the basis of risk of bias of the included studies, inconsistency, indirectness, imprecision of data, and publication bias. We used GRADEpro GDT software to prepare the 'Summary of findings' tables and the [Ryan 2016](#) publication to prepare GRADE ratings ([GRADEpro GDT 2015](#)).

RESULTS

Description of studies

Results of the search

See [Figure 1](#).

Figure 1. Study flow diagram.

Included studies

We added one additional study in the 2018 update ([Mellbring 1986](#)), resulting in a total of 20 RCTs that met the inclusion criteria ([Allan 1983](#); [Barnes 1978](#); [Bergqvist 1984](#); [Chin 2009](#); [Fredin 1989](#); [Holford 1976](#); [Hui 1996](#); [Kalodiki 1996](#); [Kierkegaard 1993](#); [Mellbring 1986](#); [Ohlund 1983](#); [Scurr 1977](#); [Scurr 1987](#); [Shirai 1985](#); [Torngren 1980](#); [Tsapogas 1971](#); [Turner 1984](#); [Turpie 1989](#); [Wille-Jorgensen 1985](#); [Wille-Jorgensen 1991](#)). See the [Characteristics of included studies](#)

table. [Mellbring 1986](#) had previously been excluded due to data issues which were overcome for this update.

All trials

The 20 included RCTs provided a total of 2853 analytic units (1681 participants and 1172 legs). Specialties involved:

- general surgery, 10 trials (Allan 1983; Bergqvist 1984; Holford 1976; Mellbring 1986; Scurr 1977; Scurr 1987; Torngren 1980; Tsapogas 1971; Wille-Jorgensen 1985; Wille-Jorgensen 1991);
- orthopaedics, six trials (Barnes 1978; Chin 2009; Fredin 1989; Hui 1996; Kalodiki 1996; Ohlund 1983);
- neurosurgery, one trial (Turpie 1989);
- cardiac surgery, one trial (Shirai 1985);
- obstetrics and gynaecology, one trial (Turner 1984); and
- cardiology, one trial (Kierkegaard 1993).

Patients undergoing general surgery formed the largest group (1486 of 2853 analytic units, 52%), followed by patients undergoing orthopaedic surgery (598 of 2853 analytic units, 21%).

All participants in the treatment groups received GCS as the method of DVT prophylaxis, with or without an additional background method of thromboprophylaxis. In nine included trials, participants in the control group received no DVT prophylaxis (Allan 1983; Chin 2009; Holford 1976; Hui 1996; Scurr 1977; Shirai 1985; Tsapogas 1971; Turner 1984; Turpie 1989). In the remaining 11 included trials, where stockings were used over a background method of thromboprophylaxis, participants in the control group received either:

- dextran 70 (Bergqvist 1984; Fredin 1989; Ohlund 1983);
- subcutaneous heparin (Torngren 1980; Wille-Jorgensen 1985; Wille-Jorgensen 1991);
- aspirin (Barnes 1978; Kierkegaard 1993);
- low molecular weight heparin (Kalodiki 1996; Mellbring 1986); or
- sequential compression (Mellbring 1986; Scurr 1987).

Participants in the treatment group also received GCS.

Methodological differences between trials

In all but one of the RCTs participants were aged 35 years and above. The exception was Turpie 1989, which involved neurosurgical patients aged 16 years and above. One trial involved participants with myocardial infarction who were aged 70 years and over (Kierkegaard 1993), and one trial involved participants undergoing cardiac surgery who were aged 18 to 81 years (Shirai 1985).

All trials used thigh-length GCS, except Hui 1996, in which one group used thigh-length stockings and another used knee-length stockings. We combined these groups for the purposes of this review. One participant in the trial by Turpie 1989 wore knee-length stockings due to obesity. Five trials did not mention the length of the stockings used (Allan 1983; Chin 2009; Ohlund 1983; Turner 1984; Wille-Jorgensen 1991).

In all trials GCS were applied either on the day of admission or on the day of operation. This was not critically evaluated on the assumption that all participants were fully mobile prior to surgery. In all but two of the trials the stockings were worn until the day of discharge or until the participants were fully mobile; participants in the remaining two studies wore GCS for 14 days or until discharge (Fredin 1989; Turpie 1989).

Most RCTs (16 of 20 trials) used the radioactive I¹²⁵ fibrinogen uptake (FUT) assay to screen for DVT postoperatively and phlebography to confirm the diagnosis. One trial used Doppler ultrasonography for screening and phlebography for confirmation

of DVT (Barnes 1978); two trials used only phlebography (Hui 1996; Kalodiki 1996); and one trial used only duplex ultrasonography for diagnosis of DVT (Chin 2009).

Excluded studies

We excluded a further six studies in the 2018 update (Barinov 2014; NCT01234064; NCT01935414; Sultan 2014; Wille-Jorgensen 1986; Zheng 2014), bringing the total number of excluded studies to 56. We excluded studies for the following reasons.

- Thirty-five studies did not have appropriate control arms (Ayhan 2013; Barinov 2014; Caprini 1983; Chandhoke 1991; Fasting 1985; Gao 2012; Hansberry 1991; KANT study; Koopmann 1985; Lacut 2005; Lee 1989; Lobastov 2013; Maksimovic 1996; Marston 1995; Maxwell 2000; NCT00333021; NCT01935414; Necioglu 2008; Norgren 1996; Nurmohamed 1996; Orken 2009; Porteous 1989; Rabe 2013; Ryan 2002; Sakon 2012; Serin 2010; Shilpa 2013; Silbersack 2004; Sobieraj-Teague 2012; Sultan 2014; Vignon 2013; Wille-Jorgensen 1986; Yang 2009; Zhang 2011; Zheng 2014).
- Two studies were not designed to assess the effectiveness of stockings in preventing DVT (Ido 1995; Rocca 2012).
- In six studies DVT was not diagnosed or assessed appropriately (Cohen 2007; Ibegbuna 1997; Manella 1981; Rasmussen 1988; Wilkins 1952; Wilson 1994).
- Five studies did not use the correct type of GCS (Flanc 1969; Patel 1988; Ramos 1996; Rosengarten 1970; Westrich 1996). Two trials used pneumatic compression (Ramos 1996; Westrich 1996); one trial used Tubigrip (Rosengarten 1970); and one trial used thick elastic compression stockings (Flanc 1969). In one French trial the type of stocking used was not clear (Patel 1988).
- Three studies did not meet the inclusion criteria of this review based on types of patients included (Belcaro 1993; CLOTS 2009; Muir 2000). One study appeared to evaluate people with recurrent DVT in the community (Belcaro 1993). Two studies evaluated people with acute stroke (CLOTS 2009; Muir 2000); these trials have been included in a separate Cochrane Review focusing on people with acute stroke (Naccarato 2010). The rationale for this is as follows: stockings reduce the cross-sectional area of the deep veins, making the calf muscle pump more effectively and thereby improving blood flow. The authors of the CLOTS trial have suggested that severe leg weakness in people with acute stroke may therefore account for the ineffectiveness of stockings in this patient group (CLOTS 2009).
- Five studies were only published as abstracts, making it difficult to accurately assess their methodology and to extract data (Bolton 1978; Brunkwall 1991; NCT01234064; Perkins 1999; Sultan 2011). Further information provided by the authors of the Sultan 2011 trial showed that not all participants in this trial had been hospitalised, therefore it did not meet our inclusion criteria.

See the [Characteristics of excluded studies](#) table for further details.

Studies awaiting classification and ongoing studies

We could not adequately assess the study design for Celebi 2001 as the report was not published in English, therefore we have categorised it as awaiting classification. See the [Characteristics of studies awaiting classification](#) table for further details.

We identified three ongoing studies ([ChiCTR1800014257](#); [GAPS](#); [IRCT2017080935594N1](#)), of which two trials are scheduled to conclude in 2019 ([GAPS](#); [IRCT2017080935594N1](#)), and one trial in late 2020 ([ChiCTR1800014257](#)). See [Characteristics of ongoing studies](#) table for further details.

Risk of bias in included studies

Details regarding risk of bias are provided in the [Characteristics of included studies](#) table and are represented in [Figure 2](#) and [Figure 3](#).

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Allan 1983	+	?	+	+	+	+
Barnes 1978	?	+	?	+	+	-
Bergqvist 1984	+	?	+	+	+	?
Chin 2009	?	?	+	+	+	+
Fredin 1989	?	?	+	+	+	+
Holford 1976	?	+	?	+	+	+
Hui 1996	?	?	?	+	+	?
Kalodiki 1996	+	+	+	+	+	?
Kierkegaard 1993	?	?	+	+	+	+
Mellbring 1986	?	+	?	+	+	+
Ohlund 1983	?	?	?	+	+	+
Scurr 1977	+	?	?	+	+	+
Scurr 1987	?	?	?	+	+	?
Shirai 1985	?	?	?	?	?	?
Torngren 1980	-	?	?	+	+	+
Tsapogas 1971	+	?	?	+	+	?
Turner 1984	+	?	+	+	+	+
Turpie 1989	?	+	+	+	+	+
Wille-Jorgensen 1985	+	?	+	+	+	+
Wille-Jorgensen 1991	+	+	?	+	+	?

Figure 3. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

Allocation

Nine trials described the method of randomisation of participants to treatment and control groups, which was done using:

- random number tables in six trials (Allan 1983; Bergqvist 1984; Tsapogas 1971; Turner 1984; Wille-Jorgensen 1985; Wille-Jorgensen 1991);
- coin toss in one trial (Scurr 1977);
- consecutively numbered boxes in one trial (Kalodiki 1996);
- date of birth in one trial (Torngren 1980), which we deemed to be an inadequate method of randomisation, and so we judged the study to be at high risk of bias.

In Tsapogas 1971, participants were randomised using a random allocation table (low risk of bias). However, there was a discrepancy between the numbers of participants randomised to the treatment and control groups, therefore we deemed this trial to be at unclear risk of bias likely due to unclear allocation concealment.

The method of randomisation was not mentioned in the remaining 11 included trials, so these trials were judged to be at unclear risk of bias (Barnes 1978; Chin 2009; Fredin 1989; Holford 1976; Hui 1996; Kierkegaard 1993; Mellbring 1986; Ohlund 1983; Scurr 1987; Shirai 1985; Turpie 1989). In Hui 1996, participants were randomised in a ratio of 1:1 in the thigh-length GCS group and 1:4 in the knee-length GCS group. The control group of the thigh-length GCS group was also used as the control for the knee-length GCS group in this trial.

Of note, Chin 2009 was the only included trial published after the publication of the CONSORT statement in 1996 (CONSORT 1996). Despite this, the Chin 2009 trial report did not include a power calculation and did not report the method of randomisation and use of allocation concealment, as advised in the CONSORT statement, suggesting risk of bias.

There was no mention of allocation concealment in 14 of the 20 RCTs judged as at unclear risk of bias. The remaining six studies used sealed envelopes to conceal the allocation of participants to

the treatment and control groups and were judged as at low risk of bias (Barnes 1978; Holford 1976; Kalodiki 1996; Mellbring 1986; Turpie 1989; Wille-Jorgensen 1991).

Blinding

It is inherently difficult to ensure adequate blinding for patients who wear stockings and those who do not. In eight trials, the radiologist reporting the scan results was unaware of whether the participant, or their leg, belonged to the treatment or control group, so these were judged as at low risk of bias (Allan 1983; Bergqvist 1984; Chin 2009; Kalodiki 1996; Turner 1984; Turpie 1989; Wille-Jorgensen 1985; Wille-Jorgensen 1991). In two trials the results of the studies were analysed without knowledge of the type of prophylaxis, so these were also judged as at low risk of bias (Fredin 1989; Kierkegaard 1993). We judged the remaining 10 studies as at unclear risk of performance and detection bias (Bergqvist 1984; Holford 1976; Hui 1996; Mellbring 1986; Ohlund 1983; Scurr 1977; Scurr 1987; Shirai 1985; Torngren 1980; Tsapogas 1971).

Incomplete outcome data

In seven trials, results for all included participants were analysed (Barnes 1978; Chin 2009; Kierkegaard 1993; Scurr 1987; Tsapogas 1971; Turner 1984; Turpie 1989). In the remaining trials, participants lost to follow-up were accounted for, with some participants excluded postrandomisation due to failure to comply with wearing the GCS because they found them uncomfortable. One trial did not report participant attrition during the study period (Shirai 1985), but this report could not be accurately appraised as it was published in Japanese and was therefore found to be at unclear risk of bias. We judged the remainder of the studies as at low risk of bias.

Selective reporting

All included studies reported the incidence of DVTs as stated in their aims. Visual inspection of the funnel plot showed that all included trials came within the expected confidence intervals, though there was a suggestion of minimal publication bias (Figure 4). We found one study to be at unclear risk of bias as it was published in

Japanese and we were unable to accurately appraise this report (Shirai 1985). The remainder of the studies were judged as at low risk of bias.

Figure 4. Funnel plot of comparison: Incidence of DVT with stockings and without stockings (all specialties).

Other potential sources of bias

None of the trials stratified participants according to DVT risk level. However, our own analysis of the papers indicated that all participants were in either moderate- or high-risk groups.

Six trials obtained funding or support from pharmaceutical companies or manufacturers of GCS, and we were unclear if this could have influenced the studies. These companies included The Kendall Company (Barnes 1978; Scurr 1987; Wille-Jorgensen 1991), Beiersdorf AB (Bergqvist 1984), Brevet Hospital Products (Hui 1996), and Rhone-Poulenc Rorer (Kalodiki 1996).

In addition, Barnes 1978 was terminated early as it was deemed unjustifiable to continue after revealing a major incidence of DVT amongst participants who did not wear stockings; we assessed this study as being at high risk of bias.

In one trial (Tsapogas 1971), participants in the treatment group were given an additional recommendation regarding exercise that was not given to the control group. It is possible this influenced the risk of thrombosis, therefore we judged this study as at unclear risk of bias.

One trial was published in Japanese (Shirai 1985), which made it difficult to accurately appraise the study design.

Effects of interventions

See: [Summary of findings for the main comparison](#) Graduated compression stockings for prevention of deep vein thrombosis - all patients; [Summary of findings 2](#) Graduated compression stockings for prevention of deep vein thrombosis in surgical patients; [Summary of findings 3](#) Graduated compression stockings for prevention of deep vein thrombosis in medical patients

The results of the review should be interpreted with caution, paying particular attention to the detailed notes in the [Description of studies](#) section, as these may have influenced the analysis due to variations within the included trials, for example the use of the opposite limb as the control, differing background prophylactic methods used, and the age difference in some of the trials. However, in the majority of the included trials a statistically significant difference between the treated participants (those that used GCS) and the control group (those that did not use GCS) was demonstrated in the incidence of DVT (primary outcome).

Incidence of DVT

In the 2014 update, we merged trials assessing the effectiveness of GCS as the sole method of prophylaxis together with trials using a background method of thromboprophylaxis for all participants in addition to the use of GCS in the treatment group. This resulted in a total of 2853 analytic units (1681 individual participants and 1172 individual legs) in the meta-analysis (Analysis 1.1). In the treatment group (GCS), 134 of the 1445 units developed DVT in comparison to 290 of the 1408 units in the control group (no GCS): Peto's odds ratio (OR) of 0.35 (95% confidence interval (CI) 0.28 to 0.43; 2853 units; 20 studies; $P < 0.001$; high-quality evidence). This amounted to a 9% incidence of DVT in the treatment group in comparison to a 21% incidence in the control group.

The I^2 statistic for this analysis suggested 10% heterogeneity, with $P = 0.33$ (Analysis 1.1). This was supported by the corresponding forest plot (Figure 4), using Peto's ORs, which showed that results for all studies were within or on the 95% CI, suggesting minimal publication bias.

Subgroup analysis by specialty

We performed subgroup analysis based upon the specialty under which the participants were managed (Figure 5). There was no significant difference between specialty subgroups regarding the effectiveness of stockings in reducing the incidence of DVT ($P = 0.15$).

Figure 5. Number of analytic units from each specialty included in the meta-analysis.

The majority of participants were general surgical patients, accounting for 1486 of 2853 units (52%). Amongst this cohort, the incidence of DVT was 52 of 741 (7%) in the treatment group and 148 of 745 (20%) in the control group (Peto OR 0.30, 95% CI 0.22 to 0.41; 1486 units; 10 studies; high-quality evidence) (Allan 1983; Bergqvist 1984; Holford 1976; Mellbring 1986; Scurr 1977; Scurr 1987; Torngren 1980; Tsapogas 1971; Wille-Jorgensen 1985; Wille-Jorgensen 1991).

Participants undergoing orthopaedic surgery accounted for 598 of 2853 units (21%) (Barnes 1978; Chin 2009; Fredin 1989; Hui 1996; Kalodiki 1996; Ohlund 1983). Amongst participants undergoing orthopaedic surgery, 70 of 314 units (22%) in the treatment group and 97 of 284 units (34%) in the control group developed DVT (Peto OR 0.47, 95% CI 0.32 to 0.68; 598 units; 6 studies; high-quality evidence) (Analysis 1.1).

The four remaining trials on participants from other specialties provided small sample sizes for each of the specialties (Kierkegaard 1993; Shirai 1985; Turner 1984; Turpie 1989). Combining the results favoured the use of stockings (Peto OR 0.28, 95% CI 0.16 to 0.48; 769 participants; 4 studies; moderate-quality evidence). Of note, only one trial considered medical patients (Kierkegaard 1993), making it difficult to confidently judge the effect of stockings in these participants (Analysis 1.1).

Subgroup analysis to compare all surgery versus medical did not reveal any differences in DVT incidence ($P = 0.15$). Combining results from 19 trials focusing on surgical patients, 134 of 1365 units (9.8%) developed DVT in the GCS group compared to 282 of 1328 units (21.2%) in the control group. The Peto OR was 0.35 (95% CI 0.28 to 0.44; $P < 0.001$; high-quality evidence), with an overall effect favouring treatment with GCS (Analysis 1.2).

Based on the results from one trial focusing on medical patients admitted following acute myocardial infarction (Kierkegaard 1993), 0 of 80 legs (0%) developed DVT in the GCS group compared to 8 of 80 legs (10%) in the control group. The Peto OR was 0.12 (95% CI 0.03 to 0.51; $P = 0.004$; low-quality evidence), with an overall effect favouring treatment with GCS (Analysis 1.2).

Incidence of proximal DVT

Proximal DVTs, which occur in the popliteal, femoral, and iliac veins, are considered to be of greatest clinical significance as they are more likely to embolise to the pulmonary veins and can thereby potentially result in fatal PE. We therefore assessed the incidence of proximal DVT in the two experimental arms of the included trials. Eight trials provided data for the incidence of proximal DVT amongst 1035 included units (Barnes 1978; Bergqvist 1984; Chin 2009; Fredin 1989; Kalodiki 1996; Kierkegaard 1993; Scurr 1987; Turpie 1989). The incidence of proximal DVT was 7 of 517 units (1%) in the treatment group and 28 of 518 units (5%) in the control group (Peto OR 0.26, 95% CI 0.13 to 0.53; 1035 units; 8 studies; $P < 0.001$; moderate-quality evidence). There was no significant difference between surgical subgroup specialities regarding the effectiveness of stockings in reducing the incidence of proximal DVT ($P = 0.79$) (Analysis 2.1).

We carried out subgroup analysis investigating differences between surgical and medical patients. Results from seven included studies evaluating surgical patients showed the incidence of proximal DVT as 7 of 437 units (1.6%) in the GCS group and 28 of 438 units (6.4%) in the control group (Barnes 1978; Bergqvist 1984; Chin 2009; Fredin 1989; Kalodiki 1996; Scurr 1987; Turpie 1989). The Peto OR was 0.26 (95% CI 0.13 to 0.53; 875 units; $P < 0.001$; moderate-quality evidence), with an overall effect favouring treatment with GCS. We downgraded the evidence for proximal DVT due to low event rate (imprecision). No events of proximal DVT were recorded in the one study involving medical patients (Analysis 2.2) (Kierkegaard 1993).

Incidence of PE

Five trials, all based on surgical patients, provided data for the incidence of PE amongst 569 included participants (Barnes 1978; Chin 2009; Holford 1976; Kalodiki 1996; Wille-Jorgensen 1985). Routine screening for PE was only conducted in two of these studies using perfusion-ventilation scintigraphy (Holford 1976; Kalodiki 1996). This method was used to confirm clinically apparent PE in the remaining studies, except in one trial where PE was diagnosed at autopsy (Turpie 1989). The incidence of PE was 5 of 283 participants (2%) in the treatment group and 14 of 286 participants (5%) in the control group (Peto OR 0.38, 95% CI 0.15 to 0.96; 569 participants; 5 studies; $P = 0.04$; low-quality evidence). These results should be interpreted with caution in light of the aforementioned limitations in reporting of the incidence of PE in the included trials. (Analysis 3.1).

One further trial reported that one participant was diagnosed with PE at autopsy but did not state to which group this participant belonged (Turpie 1989). However, the cause of death of this participant was found to be cerebral oedema. Two further trials reported a cumulative incidence of three cases of PE but did not specify to which group these participants belonged (Bergqvist 1984; Fredin 1989). Torngren 1980 reported that no participants suffered fatal PE. There was no significant difference between subgroups regarding the effectiveness of stockings in reducing the incidence of PE ($P = 0.76$). (Analysis 3.1).

Adverse effects and complications from GCS

Seven of 20 trials mentioned the incidence of adverse effects, but none of the trials stated to which groups the participants belonged (Bergqvist 1984; Chin 2009; Fredin 1989; Kalodiki 1996; Kierkegaard 1993; Torngren 1980; Wille-Jorgensen 1991).

Kierkegaard 1993 reported that some participants experienced postphlebotic changes. Four trials mentioned the incidence of bleeding associated with the background antithrombotic measure used (Bergqvist 1984; Fredin 1989; Kalodiki 1996; Wille-Jorgensen 1991). Kalodiki 1996 reported no difference in haemorrhagic complications between the treatment and control groups. One trial reported that none of the participants showed any signs of postoperative haemorrhage or side effects (Torngren 1980). Similarly, one further trial reported no adverse events related to the use of GCS (Chin 2009).

Two further trials reported participants' complaints (Hui 1996; Turpie 1989). In one trial, 23% of participants wearing above-knee stockings and 16% of participants wearing below-knee stockings found the stockings too uncomfortable and requested their removal (Hui 1996). Ambulant patients in another trial reported disturbance as the stockings fell down easily, which was likely to be due to improper fitting (Turpie 1989).

DISCUSSION

Summary of main results

Meta-analysis of the 20 included RCTs showed high-quality evidence that application of GCS decreased the occurrence of DVT in hospitalised patients (Analysis 1.1).

Eight trials reported the incidence of proximal DVT (Barnes 1978; Bergqvist 1984; Chin 2009; Fredin 1989; Kalodiki 1996; Kierkegaard 1993; Scurr 1987; Turpie 1989), and five trials reported the incidence of PE (Barnes 1978; Chin 2009; Holford 1976; Kalodiki 1996; Wille-Jorgensen 1985). A lower incidence of proximal DVT (moderate-quality evidence) and PE (low-quality evidence) was noted amongst participants fitted with GCS (Analysis 2.1; Analysis 3.1), however the low incidence rate coupled with a relatively small sample size limits the power of these meta-analyses, thereby making it difficult to confidently infer the effectiveness of GCS in preventing these outcomes.

Few adverse events were reported. In one trial some participants removed their stockings earlier than they should have done, presumably due to discomfort (Hui 1996). No other trials reported complications associated with wearing stockings. In one trial some participants developed postphlebotic changes (Kierkegaard 1993). In contrast, four studies mentioned bleeding complications related to the associated use of heparin, dextran, or aspirin, but the numbers were too small and not uniform enough to make any definitive judgement (Bergqvist 1984; Fredin 1989; Kalodiki 1996; Mellbring 1986; Wille-Jorgensen 1991).

Overall completeness and applicability of evidence

This review included predominantly patients undergoing general surgical and orthopaedic surgical procedures (Figure 5), and thus provides good evidence for the use of GCS amongst these patient groups. However, only one RCT included hospitalised medical patients, and no trial included participants deemed to have low risk

of developing DVT ([Kierkegaard 1993](#)), hence we cannot comment on the benefits of using GCS in these patient groups.

The available evidence was based predominantly on the use of above-knee stockings. Only [Hui 1996](#) looked at the difference between thigh-length GCS versus no stockings and knee-length GCS versus no stockings. In six trials, the length of the GCS used was not made explicit ([Allan 1983](#); [Chin 2009](#); [Kierkegaard 1993](#); [Ohlund 1983](#); [Turner 1984](#); [Wille-Jorgensen 1991](#)). The numbers were too small to draw any conclusions as to the efficacy of DVT prevention based on the length of the stockings used. This is not the remit of this review but is the subject of another Cochrane Review, which reported insufficient high-quality evidence to determine whether knee-length and thigh-length stockings differ in their effectiveness in reducing the incidence of DVT in hospitalised patients ([Sajid 2012](#)).

Duration of routine follow-up was 7 to 14 days, or until discharge, with a single study routinely screening for symptomatic DVT at 30-day follow-up ([Chin 2009](#)). This contrasts with epidemiological data, which demonstrates the greatest risk of postoperative DVT at four to six weeks after surgery ([Sweetland 2009](#)). The lower duration routine follow-up in the included studies does not cover this period of increased DVT risk and thus fails to accurately estimate the true magnitude of the effect of GCS in preventing DVT following discharge into the community.

None of the RCTs were uniform in detailing or recommending the duration of time that GCS should be worn postoperatively, that is until discharge, mobilisation, or the next clinic visit. This aspect is important because we know from clinical experience that DVT can still occur at home after discharge, and there have been a number of incidences of death after discharge that were due to DVT and PE. This is further supported by the results from the Million Women Study ([Sweetland 2009](#)).

Some of these areas of uncertainty have been addressed in the published protocol of an ongoing study ([GAPS](#)), where hospitalised surgical patients will receive thromboprophylaxis (low molecular weight heparin (LMWH) only versus LMWH and GCS), with the primary outcome as incidence of DVT at 90-day follow-up. In light of the increased use of chemoprophylaxis for DVT, this trial aims to specifically evaluate the additional benefit of GCS over LMWH as thromboprophylaxis. We will evaluate the final report of this study for inclusion in this review when it is available.

Quality of the evidence

We have included 20 RCTs of good methodological quality providing 2853 analytic units in this meta-analysis to determine the effectiveness of the use of GCS in hospitalised patients ([Analysis 1.1](#)). This sample size provides high-quality evidence to support the use of GCS to prevent DVT in the clinical setting, especially amongst surgical patients, since most included participants underwent either general surgical or orthopaedic surgical procedures ([Figure 5](#)). Moderate-quality evidence suggests that GCS may prevent proximal DVT; we downgraded the quality of the evidence due to imprecision. We found low-quality evidence for GCS in preventing PE, downgrading the evidence as routine screening for PE was done in only two of the five RCTs reporting on this outcome, and results were inconsistent. Only one included trial considered hospitalised medical patients, making it difficult to form a judgement regarding this subgroup of patients ([Kierkegaard 1993](#)).

Furthermore, small sample sizes limited subgroup analysis based on type of procedure, length of stockings used, or type of background prophylaxis. We were unable to confidently assess the variation in effectiveness of GCS over these parameters.

Potential biases in the review process

Interestingly, all but one of the 20 included trials were conducted before the CONSORT guidelines for reporting RCTs were published ([CONSORT 1996](#)). Most importantly, 11 of 20 trials either did not report sufficiently or used an inappropriate method of randomisation (see the [Risk of bias in included studies](#) section). We therefore performed a sensitivity analysis to assess the associated potential risk of bias, which found no significant difference in the effectiveness of stockings in reducing the incidence of DVT amongst trials that reported an appropriate method of randomisation and those that did not ($P = 0.78$, [Analysis 4.1](#)).

Seven of the 20 included RCTs involved the use of the other leg as the control ([Bergqvist 1984](#); [Kierkegaard 1993](#); [Mellbring 1986](#); [Scurr 1977](#); [Scurr 1987](#); [Shirai 1985](#); [Torngren 1980](#)). It is possible that GCS applied to one leg could have an effect on the other leg of the same patient ([Spiro 1970](#)), although there is no clear evidence for this. If this is true, it may bias the results of these studies. None of the included studies randomising individual legs reported the use of a matched or paired analysis to address statistical bias due to ignoring the pairing. This could result in these studies receiving too little weight in the meta-analysis due to wider confidence intervals, and thereby possibly disguising clinically important heterogeneity ([Higgins 2011](#)). However, since the studies are underweighted rather than overweighted, the analysis is conservative. Despite such concerns, all these trials have demonstrated that GCS reduced the risk of DVT compared to when GCS were not applied. A sensitivity analysis performed to assess this further found stockings to be effective in reducing the incidence of DVT irrespective of whether the unit of randomisation was individual legs or individual participants ([Analysis 4.2](#)). In other words, there was no difference in the effectiveness of stockings in reducing the incidence of DVT irrespective of the unit of randomisation ($P = 0.24$).

As part of a previous update, we merged trials using stockings as the sole method of thromboprophylaxis and those using stockings over a background method of thromboprophylaxis, thereby introducing a potential bias. However, both these groups of trials demonstrated a reduced incidence of DVT, with or without a background method of thromboprophylaxis ([Analysis 4.3](#)), with no clear difference in the magnitude of effect ($P = 0.25$). It must be stressed that results for the use of GCS over a background method of thromboprophylaxis should be interpreted with some caution, as this group of trials was heterogeneous. Background prophylaxis varied between dextran 70, heparin, aspirin, and sequential compression. We could not assess the extent of influence of individual background prophylaxis since further grouping would have reduced the number of participants so much that the data would not be valid.

[Flordal 1995](#) and [Lensing 1993](#) have previously highlighted poor efficacy of using radioactive 125 I fibrinogen uptake test (FUT) as the only diagnostic modality for DVT. In this review, eight of the 20 included trials relied solely on FUT to diagnose DVT. We therefore performed a sensitivity analysis to assess the associated potential risk of bias by the inclusion of these studies ([Analysis 4.4](#)), which found that results of trials using phlebography to confirm the diagnosis of DVT following a positive FUT and those using

other modalities for the diagnosis of DVT (ultrasonography, or phlebography alone) also strongly favoured the use of stockings in diminishing the risk of DVT. There was no significant difference in the effectiveness of stockings in reducing the incidence of DVT between subgroups of diagnostic modalities ($P = 0.29$).

After excluding stroke patients, we identified only one RCT that involved a medical specialty, which was in patients following a myocardial infarction (Kierkegaard 1993). It was thus difficult to confidently judge the effectiveness of GCS in preventing DVT in

medical patients, and further trials are required in this cohort of patients.

It is important to note that visual interpretation of the funnel plot demonstrated a borderline risk of publication bias in assessing the effectiveness of stockings in preventing DVT (Figure 4; Analysis 1.1). However, we noted no clear evidence of publication bias in meta-analyses of the incidence of proximal DVT and PE (Figure 6; Figure 7).

Figure 6. Funnel plot of comparison: Incidence of proximal DVT with stockings and without stockings (all specialties).

Figure 7. Funnel plot of comparison: Incidence of PE with stockings and without stockings (all specialties).

Agreements and disagreements with other studies or reviews

Results from this review are comparable to those of a previous health technology assessment ([Roderick 2005](#)), which found a 66% risk reduction with the application of GCS and a 60% risk reduction when GCS were used on a background of another prophylactic method. The variation in the degree of risk reduction reported by that review, as compared to our results, may be because their analyses were based upon the number of participants originally randomised in the included trials and included participants who were later excluded (i.e. an intention-to-treat analysis). Furthermore, a number of trials included in [Roderick 2005](#) did not meet our inclusion criteria.

The National Institute for Health and Care Excellence (NICE) has published guidance for reducing the risk of venous thromboembolism amongst hospitalised patients ([NICE 2010](#)). Their recommendations are consistent with our finding that GCS are more effective than no prophylaxis. However, NICE recommends that GCS should not be prescribed to patients admitted for stroke; this was based primarily on the [CLOTS 2009](#) trial in which large proportions of patients were prescribed aspirin, which may have influenced the results. It also raises the issue of lack of evidence concerning the use of mechanical prophylaxis in medical patients.

AUTHORS' CONCLUSIONS

Implications for practice

We found high-quality evidence that graduated compression stockings (GCS) are effective in reducing the risk of deep vein thrombosis (DVT) in hospitalised patients who have undergone general and orthopaedic surgery, with or without other methods of background thromboprophylaxis, where clinically appropriate. We found moderate-quality evidence that GCS probably reduce the risk of proximal DVT and low-quality evidence that GCS may reduce the risk of pulmonary embolism. There remains a paucity of evidence to assess the effectiveness of GCS in diminishing risk of DVT in medical patients.

Implications for research

There is scope for further research in this field:

- studies are needed to evaluate whether specific target groups such as patients with malignancy, a past history of DVT, or hypercoagulable states would benefit from the use of GCS;
- amongst trials included in this review, participants were followed up for a period of 7 to 14 days, or until discharge. However, since the risk of DVT is greatest at four to six weeks postoperatively, studies are needed to investigate the duration of DVT prophylaxis required to prevent DVT episodes at home after discharge from hospital;

- none of the included randomised controlled trials specifically addressed complications associated with the use of GCS. This needs to be examined further, particularly in specific groups such as orthopaedic patients, because concerns have been raised that consequent complications may outweigh the benefits of GCS if they are worn improperly;
- randomised controlled trials are needed:
 - in patients with medical illness as opposed to surgical illness;
 - to compare above-knee with below-knee GCS;
 - to compare GCS against other methods of prophylaxis;
 - to evaluate effectiveness of GCS in preventing venous thromboembolism-associated mortality.
- finally, the cost implications for any health service providers, and comparison with other methods, need to be assessed.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Allan 1983

Methods	<p>Study: RCT Exclusions postrandomisation: 11 Losses to follow-up: 0 DVT diagnosis: FUT. Scanned on first, second, third, fifth, and seventh day after operation. In participants with evidence of DVT, scanning was continued until the participant left the hospital. Phlebogram performed if evidence of DVT to assess proximal involvement.</p> <p>Follow-up: 7 days Statistical analysis: Chi² test</p>
Participants	<p>Country: UK Total number of participants: 211 Total available for analysis: 200 Age: > 40 years</p> <p>Sex: male and female Inclusion criteria: abdominal surgery greater than 30 minutes duration Exclusion criteria: past DVT, PE, varicose veins, steroid or anticoagulant therapy</p>
Interventions	<p>Type of treatment: GCS length not stated Control: 103 Treatment: 97 Duration: GCS fitted on the evening before the operation and continued until 7 days thereafter.</p>
Outcomes	<p>DVT Control: 37 Treatment: 15 P < 0.025</p> <p>PE: not mentioned</p>
Notes	<p>Benign and malignant patients were differentiated as follows.</p> <p>Benign Control: 51, DVT: 16 Treatment: 49, DVT: 5 P < 0.058</p> <p>Malignant Control: 52, DVT: 21 Treatment: 48, DVT: 10 P < 0.05</p> <p>Incidence of proximal DVT not reported.</p>

Allan 1983 (Continued)

No adverse events were reported.

The Kendall Company supplied the stockings and fibrinogen in the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were allocated using random number series.
Allocation concealment (selection bias)	Unclear risk	Method of concealment not described.
Blinking (performance bias and detection bias) All outcomes	Low risk	"The scans were assessed without reference to patient or group." Comment: probably done
Incomplete outcome data (attrition bias) All outcomes	Low risk	11/211 participants were not analysed, but were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcomes were reported.
Other bias	Low risk	No other source of bias identified.

Barnes 1978

Methods	Study: RCT Exclusions postrandomisation: 0 Losses to follow-up: 0 DVT diagnosis: Doppler ultrasound on alternate days until discharge. Venography if positive and lung perfusion scan if venography substantiates or on clinical manifestation of chest pain PE diagnosis: only participants with clinical manifestations of PE were evaluated with chest X-rays, arterial blood gases, and perfusion lung scanning. Statistical analysis: Fisher exact probability Follow-up: "until discharge"
Participants	Country: USA Total number of participants: 18 Total available for analysis: 18 Age: > 50 years Sex: male and female Inclusion criteria: all patients admitted for hip operation Exclusion criteria: none
Interventions	Type of treatment: GCS thigh length Additional background thromboprophylaxis: aspirin Control: 10 Treatment: 8 Duration: GCS fitted on the day of surgery until discharge.
Outcomes	DVT (all) Control: 5

Barnes 1978 (Continued)

Treatment: 0
P = 0.029

Proximal DVT

Control: 4
Treatment: 0
P not reported

Symptomatic PE (confirmed by lung perfusion scan)*

Control: 3
Treatment: 0

*Evaluation of PE using lung perfusion scans was only performed in participants with clinical manifestations of PE.

Notes	<p>Some participants had:</p> <ul style="list-style-type: none"> • aspirin during the study; • previous DVT; • previous leg injuries; • varicose veins; • venous skin changes. <p>Study was stopped due to an increased incidence of DVT in the control group. All 3 participants with radiographically confirmed PEs were also noted as having DVTs. Incidence of adverse events not mentioned.</p>
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not mentioned.
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 18 participants were accounted for and included in the analysis.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	High risk	<p>This study was terminated early. "It was considered medically unjustifiable to continue this study when a significantly greater incidence of major deep vein thrombosis developed in the patients not wearing stockings."</p> <p>Also, authors of this study were awarded a grant from the Kendall Research Center, who manufacture stockings.</p>

Bergqvist 1984

Methods	Study: RCT
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Bergqvist 1984 (Continued)

	<p>Exclusions postrandomisation: 8</p> <p>Losses to follow-up: 0</p> <p>DVT diagnosis: FUT. Scanned first and subsequently every second day</p> <p>Follow-up: 7 days for DVT, 30 days for fatal PE or postoperative complications</p> <p>Statistical analysis: exact binomial test</p>
Participants	<p>Country: Sweden</p> <p>Total number of participants: 88</p> <p>Total available for analysis: 80</p> <p>Age: 50 years</p> <p>Sex: male and female</p> <p>Inclusion criteria: all abdominal operations</p> <p>Exclusion criteria: < 50 years of age</p>
Interventions	<p>Type of treatment: GCS thigh length</p> <p>Additional background thromboprophylaxis: dextran 70</p> <p>Control: 80 (39 right leg and 41 left leg)</p> <p>Treatment: 80 (41 right leg and 39 right leg)</p> <p>Duration: evening before the operation until the seventh postoperative day</p>
Outcomes	<p>DVT (all)</p> <p>Control: 8</p> <p>Treatment: 0</p> <p>P < 0.01</p> <p>Proximal DVT</p> <p>Control: 1</p> <p>Treatment: 0</p> <p>P not reported</p>
Notes	<p>This study included the infusion of dextran 70 as prophylactic measure in addition to stockings in both groups; non-stockinged legs acted as control.</p> <p>1 participant had symptoms of PE.</p> <p>Adverse events: bleeding complications reported in 4 participants, but no adverse events associated with GCS were reported.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"using a random number table"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Low risk	"When analysing the data from the fibrinogen test, it was not clear which leg was stockinged."
Incomplete outcome data (attrition bias) All outcomes	Low risk	8/80 participants were not analysed, but were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.

Bergqvist 1984 (Continued)

Other bias	Unclear risk	The study was partly funded by a grant from Beiersdorf AB, who also supplied the compression stockings.
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Chin 2009

Methods	<p>Study: RCT</p> <p>Exclusions postrandomisation: 0</p> <p>Losses to follow-up: 0</p> <p>DVT diagnosis: bilateral duplex ultrasonography (frequency of investigation unspecified)</p> <p>PE diagnosis: ventilation-perfusion scanning or spiral computed tomography of the chest, or both</p> <p>Follow-up: 1 month</p> <p>Statistical analysis: Chi² test</p>
Participants	<p>Country: Singapore</p> <p>Total number of participants: 440</p> <p>Total available for analysis: 440. Of these, 220 participants from 2 experimental groups (no prophylaxis and GCS only) were eligible for inclusion in our review.</p> <p>Age: 47 to 85 years</p> <p>Sex: male and female</p> <p>Inclusion criteria: low-risk patients undergoing elective total knee arthroplasty with no known predisposition to thromboembolism</p> <p>Exclusion criteria: use of anticoagulants or aspirin, history of PE or DVT in the previous year, BMI > 30 kg/m², preoperative prolonged immobilisation or being wheelchair bound, bleeding tendency or a history of GI bleeding, surgery in the previous 6 months, cerebrovascular accident in the previous 3 months, uncontrolled hypertension, congestive cardiac failure, renal or liver impairment, allergy to heparin or heparin-induced thrombocytopenia, varicose veins or CVI, PVD, skin ulcers, dermatitis, or wounds, and malignancy</p>
Interventions	<p>Type of treatment: GCS applied to legs (length unspecified)</p> <p>Control: 110 (group 1)</p> <p>Treatment: 110 (group 2)</p> <p>Duration: applied until day 5 to 7 or stopped earlier if participants were suspected as having DVT or PE based on bilateral duplex ultrasonography</p>
Outcomes	<p>DVT (all)</p> <p>Control: 24 (3 proximal, 21 distal)</p> <p>Treatment: 14 (1 proximal, 13 distal)</p> <p>P = 0.119</p> <p>Proximal DVT</p> <p>Control: 3</p> <p>Treatment: 1</p> <p>Symptomatic PE</p> <p>Control: 1</p> <p>Treatment: 1</p>
Notes	<p>Participants were divided into 4 experimental groups consisting of 110 participants each: no prophylaxis, GCS only, IPC only, and LMWH only. Only patients at low risk of developing VTE were included.</p> <p>Standardised rehabilitation protocols were used, with continuous passive movements initiated on day 2 and ambulation on day 3 postoperatively.</p>

Chin 2009 (Continued)

Adverse events: no adverse effects such as skin rash, swelling above the appliance, pressure necrosis of the skin, or peroneal nerve palsy related to the use of GCS and IPC. At 1-month follow-up, 2 participants each in the control and GCS group were readmitted due to superficial wound infections.

Funding source was not disclosed.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Low risk	Single-blinded. "Bilateral duplex ultrasonography (carried out by one of 3 dedicated ultrasonographers blinded to the prophylactic method used)."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 440 participants were accounted for and analysed.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Low risk	No other sources of bias identified.

Fredin 1989

Methods	Study: RCT Exclusions postrandomisation: 6 Losses to follow-up: 0 DVT diagnosis: FUT on first and every alternate day for 10 days Follow-up: phlebography at 10 days, clinical follow-up regarding fatal PE and postoperative complications up to 30 days Statistical analysis: Student's t-test
Participants	Country: Sweden Total number of participants: 150 Total available for analysis: 144 Age: > 40 years Sex: male and female Inclusion criteria: all patients for total hip arthroplasty Exclusion criteria: swelling of legs, leg ulcers, eczema, malignancy, varicose veins, previous DVT, previous PE, and cardiovascular diseases
Interventions	Type of treatment: GCS thigh length Additional background thromboprophylaxis: dextran 70 Control: 48 Treatment: 49 Duration: applied on the evening before the operation for 14 days
Outcomes	DVT (all, unit of analysis = individual legs)

Fredin 1989 (Continued)

Control: 13 of 47
Treatment: 3 of 49
P < 0.01

Proximal DVT (unit of analysis = individual legs)

Control: 9 of 47
Treatment: 1 of 49

Symptomatic PE (confirmed by scintigraphy)

Control: 2
Treatment: 0
P not reported

Notes

All participants had regular dextran 70 prophylaxis.

Individual participants were randomised to the 3 treatment groups. However, we included only the non-operated leg's values in our analysis because in these orthopaedic patients thrombotic process may have already been initiated during surgery.

Incidence of symptomatic DVT not reported.

Adverse events: 2 participants reported discomfort and discontinued wearing stockings after 2 days. Incidence of bleeding reported, which might have been associated with low-dose heparin: 3 wound haematomas and minor bleeding from gastric drainage in 1 participant. A further 7 participants were withdrawn from the trial due to bleeding, which might also have been due to heparin.

Funded by Swedish Medical Research Council

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Low risk	"The data was analysed blindly concerning the type of prophylaxis."
Incomplete outcome data (attrition bias) All outcomes	Low risk	6/150 participants were not included in analysis, but were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Low risk	No other sources of bias identified.

Holford 1976

Methods

Study: RCT
Exclusions postrandomisation: 3
Losses to follow-up: 0
DVT diagnosis: FUT on day prior to surgery and every day postoperatively for 6 to 7 days
Follow-up: 6 to 7 days

Holford 1976 (Continued)

Statistical analysis: Chi² test with Yates' correction

Participants	Country: UK Total number of participants: 98 Total available for analysis: 95 Age: > 40 years Sex: male and female Inclusion criteria: > 40 years of age. Major abdominal, pelvic, or thoracic surgery Exclusion criteria: none mentioned
Interventions	Type of treatment: GCS thigh length Control: 47 Treatment: 48 Duration: applied 12 hours before surgery, and removed after participant was fully mobile (4 to 5 days later). Participants were encouraged to mobilise early.
Outcomes	DVT Control: 23 Treatment: 11 P < 0.01 Symptomatic PE* (confirmed by lung scanning) Control: 1 Treatment: 0 *Incidence of PE was not routinely assessed in all participants.
Notes	Adverse events: not mentioned Incidence of proximal DVT not reported. The source of funding was not disclosed. However, stockings were provided by The Kendall Company, which manufactures stockings.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients were allocated randomly" Comment: no mention of how this was achieved
Allocation concealment (selection bias)	Low risk	"Patients were allocated randomly to a stocking group or control group by instructions in sealed envelopes."
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/98 participants were not included in the analysis, but were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcomes were reported.
Other bias	Low risk	No other sources of bias identified.

Hui 1996

Methods	Study: RCT Exclusions postrandomisation: 37 Losses to follow-up: 0 DVT diagnosis: phlebography between fifth and seventh day postoperatively Follow-up: between 5 and 7 days Statistical analysis: Chi ² test, Fisher's exact test, and Student's t-test
Participants	Country: UK Total number of participants: 177 Total available for analysis: 138 Age: > 40 years Sex: male and female Inclusion criteria: all patients admitted for total hip or knee replacement Exclusion criteria: past history of DVT, PVD, revision of prosthesis, or bilateral joint replacements
Interventions	Type of treatment: GCS thigh and knee length Control (thigh length and knee length): 54 Treatment: 86 Duration: applied on the day before surgery and removed after a week
Outcomes	DVT Control: 30 Treatment: 38 P not reported
Notes	Analysis of participants was performed between those who received above-knee and those who received below-knee stockings. Both operated and non-operated legs were analysed separately. Method of randomisation is not clear, although it appears to be appropriate. Incidence of proximal DVT not reported. 1 fatal PE in knee replacement control group. Participants were not routinely assessed for presence of PE. Incidence of adverse events not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not mentioned. Participants were randomised in a ratio of 1:1 in the thigh-length GCS group and 1:4 in the knee-length GCS group.
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	39/177 participants were not analysed, but were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcomes were reported.

Hui 1996 (Continued)

Other bias	Unclear risk	The control group of the thigh-length GCS group was also used as the control for the knee-length GCS group. Partly funded by Brevet Hospital Products, which manufactures stockings.
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Kalodiki 1996

Methods	<p>Study: RCT Exclusion to postrandomisation: 15 Losses to follow-up: 0 DVT diagnosis: venography performed on eighth to 12th postoperative day, before discharge. PE diagnosis: perfusion lung scans performed on the day before surgery and on the eighth to 12th postoperative day, before discharge.</p> <p>Follow-up: 8 to 10 days for DVT and PE (routinely) Statistical analysis: Yates' correction</p>
Participants	<p>Country: UK Total number of participants: 93 Total available for analysis: 78 Age: > 40 years</p> <p>Sex: male and female Inclusion criteria: patients having unilateral total hip replacement for the first time or without cement under general anaesthesia Exclusion criteria: patients with bleeding disorders or bleeding risks, anticoagulant therapy, NSAIDs or aspirin, cardiovascular disease, renal or hepatic or pancreatic disease, relevant allergies or hypersensitivities</p>
Interventions	<p>Type of treatment: GCS thigh length Additional background thromboprophylaxis: subcutaneous enoxaparin (LMWH) Control: 32 Treatment: 32 Duration: stockings applied on both legs before the operation until discharge.</p>
Outcomes	<p>DVT (all) Control: 12 Treatment: 8 $P > 0.1$</p> <p>Proximal DVT Control: 9 Treatment: 3* P value: not significant ($0.1 > P > 0.05$) *1 additional thrombus in the treatment group was an extension of calf thrombosis.</p> <p>PE Control: 3/29 Treatment: 2/31 P value: not significant (value not reported)</p>
Notes	<p>All participants in the treatment and control groups had enoxaparin 40 mg 12 hours before the operation, and then once daily until discharge.</p> <p>We excluded an additional group of 14 participants who received no prophylaxis (placebo group) from this review.</p> <p>Adverse effects: there were no differences in haemorrhagic complications between the 3 groups, and no adverse events were recorded.</p>

Kalodiki 1996 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were assigned consecutive numbers.
Allocation concealment (selection bias)	Low risk	Used sealed envelopes
Blinding (performance bias and detection bias) All outcomes	Low risk	"Venograms and V/Q scans were reported blindly by an independent panel of 3 and 1 radiologist respectively."
Incomplete outcome data (attrition bias) All outcomes	Low risk	15/93 participants could not be evaluated because 10 declined venography and 5 did not have it for technical reasons.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Unclear risk	This study was supported by Rhone-Poulenc Rorer.

Kierkegaard 1993

Methods	Study: RCT Exclusions postrandomisation: 0 Losses to follow-up: 0 DVT diagnosis: FUT on the second day and every second day, or every day when the results were positive. Phlebography if positive Follow-up: at least 8 days, or until they developed DVT or were discharged Statistical analysis: Fisher's exact test and 2-sided Student's t-test
Participants	Country: Sweden Total number of participants: 80 Total available for analysis: 80 Age: > 70 years Sex: male and female Inclusion criteria: all patients with myocardial infarction as defined by Minnesota Code Category 1 Exclusion criteria: none given.
Interventions	Type of treatment: GCS thigh length Additional background thromboprophylaxis: aspirin Control: 80 (opposite non-stockinged leg) Treatment: 80 Duration: time of application and duration applied were not given.
Outcomes	DVT (all) Control: 8 Treatment: 0 P = 0.0003 Proximal DVT Control: 0 Treatment: 0

Kierkegaard 1993 (Continued)

Symptomatic DVT

Control: 0

Treatment: 0

Notes	<p>1 limb was randomised to act as control. Aspirin was used in all participants.</p> <p>Incidence of PE not mentioned.</p> <p>Adverse events: postphlebitic changes</p> <p>Funded by Halmstad Hospital Foundation for Medical Research, the TRYGG-HANSA Foundation for Medical Research, and the Faculty of Medicine, Lund University. Stockings were supplied by The Kendall Health Products Company, which manufactures stockings.</p>
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Low risk	<p>"Results were calculated without knowledge of which leg had stockings and which leg developed a positive fibrinogen uptake test."</p> <p>Comment: researchers were blinded to the treatment group while calculating results, however insufficient detail was available to ascertain whether assessors were blinded at the time of FUT or phlebography, or both.</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 80 participants were accounted for and analysed.
Selective reporting (reporting bias)	Low risk	Results for all outcome measures were reported.
Other bias	Low risk	No other sources of bias identified.

Mellbring 1986

Methods	<p>Study: RCT</p> <p>Exclusions postrandomisation: 6</p> <p>Losses to follow-up:</p> <p>DVT diagnosis: I¹²⁵ fibrinogen test preoperatively, then 1, 3, 5, 7, and 9 days</p> <p>Follow-up: 9 days, or until hospitalisation ended</p> <p>Statistical analysis: Chi² test with Yates' correction and Mann-Whitney U test</p>
Participants	<p>Country: Sweden</p> <p>Total number of participants: 114 participants (1 leg from each participant randomised to GCS)</p> <p>Total available for analysis: 108 participants (216 legs)</p> <p>Age: > 50 years</p> <p>Sex: male and female</p> <p>Inclusion criteria: patients > 50 years undergoing surgery for benign or malignant abdominal disease</p>

Mellbring 1986 (Continued)

Exclusion criteria: patients with iodine hypersensitivity, on anticoagulant therapy, or with signs or symptoms of arterial insufficiency, advanced angina pectoris, or preoperatively immobile

Interventions	Type of treatment: thigh-length stockings Additional background thromboprophylaxis: dihydroergotamine + low-dose heparin (DHE-LDH) or intermittent pneumatic calf compression (IPCC) Control: 108 Treatment: 108 Duration: applied before surgery and worn until the participant was fully mobilised	
Outcomes	DVT (all) Control: 8 Treatment: 8 P not reported Proximal DVT Control: unclear Treatment: unclear Symptomatic DVT Control: unclear Treatment: unclear PE Control: not assessed Treatment: not assessed	
Notes	This study was primarily designed to compare the efficacy of DHE-LDH against IPCC, and participants were therefore randomised to either the DHE-LDH arm or the IPCC arm. Individual legs were randomised to either the GCS or the no-GCS arm, as a secondary study.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not mentioned.
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	None. Outcomes for the 6 participants who were excluded postrandomisation were reported. 2 received dextran postoperatively; 2 did not eventually receive IPCC; 1 received heparin postoperatively; and FUT was unsatisfactory in 1 further participant. Outcome data for the remaining 54 participants (108 legs) were reported.
Selective reporting (reporting bias)	Low risk	Results for all outcome measures were reported.
Other bias	Low risk	No other sources of bias identified.

Ohlund 1983

Methods	Study: RCT Exclusion to postrandomisation: 1 Losses to follow-up: 0 DVT diagnosis: FUT every day for 10 days Follow-up: 10 days Statistical analysis: Student's t-test
Participants	Country: Sweden Total number of participants: 63 Total available for analysis: 62 Age: > 50 years Sex: male and female Inclusion criteria: all patients admitted for elective hip arthroplasty Exclusion criteria: none mentioned.
Interventions	Type of treatment: GCS length not stated. Additional background thromboprophylaxis: dextran 70 Control: 31 Treatment: 31 Duration: not mentioned
Outcomes	DVT Control: 15 Treatment: 7 P < 0.05
Notes	All had dextran 70 infusion at induction of anaesthesia and 2 days following operation. Dose: 500 mL per day Incidence of proximal DVT not reported. Incidence of PE and adverse events not mentioned. Stockings were supplied by AKLA AB.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/63 participants was not analysed, but was accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Low risk	No other sources of bias identified.

Scurr 1977

Methods	Study: RCT Exclusion to postrandomisation: 5 Losses to follow-up: 0 DVT diagnosis: FUT on first, second, third, fifth, and seventh postoperative days Follow-up: 7 days Statistical analysis: Fisher's exact test
Participants	Country: UK Total number of participants: 75 Total available for analysis: 70 Age: > 42 years Sex: male and female Inclusion criteria: all patients admitted for major abdominal surgery Exclusion criteria: none mentioned.
Interventions	Type of treatment: GCS thigh length Control: 70 (32 right leg, 38 left leg) Treatment: 70 (38 right leg, 32 left leg) Duration: wore the stockings on the evening before the operation until the ninth postoperative day
Outcomes	DVT Control: 26 Treatment: 8 $P < 0.0003$
Notes	Incidences of proximal DVT, PE, and adverse events were not mentioned. Stockings were supplied by The Kendall Company.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	By "tossing a coin"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	5/75 participants were not analysed, but were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Low risk	No other sources of bias identified.

Scurr 1987

Methods	Study: RCT Exclusions postrandomisation: 0 Losses to follow-up: 0 DVT diagnosis: FUT on first, third, fifth, and seventh postoperative day and phlebography if FUT was positive Follow-up: 7 days Statistical analysis: McNemar's exact test
Participants	Country: UK Total number of participants: 78 Total available for analysis: 78 Age: > 43 years Sex: male and female Inclusion criteria: all patients admitted for abdominal operations Exclusion criteria: anyone with preoperative evidence of DVT on Doppler ultrasound and strain-gauge plethysmography methods
Interventions	Type of treatment: GCS thigh length Additional background thromboprophylaxis: sequential compression device Control: 78 (legs, sequential compression device only) Treatment: 78 (legs, sequential compression device and GCS) Duration: until ambulatory
Outcomes	DVT Control: 7 Treatment: 1 $P < 0.016$ Proximal DVT Control: 0 Treatment: 0 PE Control: 0 Treatment: 0
Notes	Left and right legs were randomised to receive either treatment or control. The control group only had a sequential compression device fitted on the day of the operation. The treatment group had both GCS and sequential compression devices fitted. Incidence of symptomatic DVT not reported. Incidence of adverse events was not mentioned. All participants wore stockings for the whole study period.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias)	Unclear risk	Not mentioned

Scurr 1987 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	All 78 participants were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Unclear risk	The study was supported in part by the Kendall Research Center.

Shirai 1985

Methods	Study: RCT Losses to follow-up: not reported DVT diagnosis: FUT and measurement of leg diameter preoperatively, immediately after surgery, and on postoperative days 1, 3, 5, and 7 Follow-up: 7 days Statistical analysis: unknown
Participants	Country: Japan Total number of participants: 126 Total available for analysis: 126 Age: 18 to 81 years (mean 54.8 years) Sex: male and female Inclusion criteria: heart surgery and vein surgery patients Exclusion criteria: complications with swellings on the veins of the legs and previous history of venous thrombosis in the legs
Interventions	Type of treatment: thigh-length GCS Control: 126 (legs with stockings) Treatment: 126 (legs without stockings) Duration: not mentioned
Outcomes	DVT Control: 17 Treatment: 5 P < 0.01
Notes	This trial was published in Japanese, which made accurate extraction of information about methodology difficult.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not stated.
Blinding (performance bias and detection bias)	Unclear risk	No mention of blinding

Shirai 1985 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Japanese study, difficult to determine
Selective reporting (reporting bias)	Unclear risk	Japanese study, difficult to determine
Other bias	Unclear risk	Japanese study, difficult to determine

Torngren 1980

Methods	Study: RCT Exclusions postrandomisation: 12 Losses to follow-up: 0 DVT diagnosis: FUT started the day before the operation up to the seventh day Follow-up: 7 days Statistical analysis: sign test
Participants	Country: Sweden Total number of participants: 110 Total available for analysis: 98 Age: > 42 years Sex: male and female Inclusion criteria: all patients admitted for major abdominal operation Exclusion criteria: those positive for preoperative FUT
Interventions	Type of treatment: GCS thigh length Additional background thromboprophylaxis: subcutaneous heparin sodium (UFH) Control: 98 Treatment: 98 Duration: GCS applied the day of the operation and continued up to sixth postoperative day.
Outcomes	DVT Control: 12 Treatment: 4 P < 0.004 Incidence of proximal DVT not reported. Incidence of PE was not routinely assessed.
Notes	All participants received heparin 5000 IU 12 hourly. No participants developed fatal PE or reported side effects. However, bleeding complications were reported, likely associated with the use of heparin. Study supported by Karolinska Institutet, Stockholm.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Randomisation was achieved "...depending on the date of birth of the patient".

Torngren 1980 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	12/110 participants were excluded from analysis, but were accounted for.
Selective reporting (reporting bias)	Low risk	Frequency of DVT in both groups was reported.
Other bias	Low risk	No other sources of bias identified.

Tsapogas 1971

Methods	Study: RCT Exclusions postrandomisation: 0 Losses to follow-up: 0 DVT diagnosis: Initially, FUT on first, third, fifth, and seventh day. Phlebography at the end of 1 week postoperatively for all participants (including those with previously negative FUT) Follow-up: 7 days Statistical analysis: not given
Participants	Country: USA Total number of participants: 95 Total available for analysis: 95 Age: > 40 years Sex: male and female Inclusion criteria: all major abdominal surgery and those who were negative to preoperative phlebography Exclusion criteria: lower limb operations, thyroid diseases
Interventions	Type of treatment: GCS thigh length Control: 44 Treatment: 51 Duration: stockings worn on the day of surgery until discharge
Outcomes	DVT Control: 6 Treatment: 2 P not reported
Notes	Numbers in each group call into question if this study was properly randomised. 2 of 6 participants who developed DVT in the control arm were noted as developing clinical signs of DVT. 1 participant developed a proximal DVT, however group allocation for this participant was not reported. Incidences of PE and adverse events were not mentioned. Participants were not routinely assessed for presence of PE.

Tsapogas 1971 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	By a random allocation table
Allocation concealment (selection bias)	Unclear risk	Not mentioned. However, there was a discrepancy between the number of participants randomised to the treatment and control groups.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 95 participants were accounted for and analysed.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Unclear risk	In addition to receiving stockings, participants in the treatment group were given extra recommendations regarding exercise that were not given to participants in the control group.

Turner 1984

Methods	Study: RCT Exclusions postrandomisation: 0 Losses to follow-up: 0 DVT diagnosis: FUT Follow-up: "until discharge" Statistical analysis: Fisher's exact test
Participants	Country: UK Total number of participants: 196 Total available for analysis: 196 Age: > 35 years Sex: female Inclusion criteria: all patients admitted for elective gynaecological surgery Exclusion criteria: malignancy, diabetes, pregnancy, DVT, anticoagulation treatment
Interventions	Type of treatment: GCS length not stated. Control: 92 Treatment: 104 Duration: GCS fitted on the day of admission. When GCS were discontinued is not mentioned.
Outcomes	DVT Control: 4 Treatment: 0 P = 0.048 PE Control: 0

Turner 1984 (Continued)

Treatment: 0

Notes

Stated as randomised, however method not made explicit. Losses to follow-up or loss to randomisation not explicit.

Incidence of proximal DVT was not reported.

Method of diagnosis of PE was not reported.

No adverse events were mentioned, and stockings were acceptable to participants, the only adverse comment being that the stockings were hot.

Stockings were supplied by The Kendall Company.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number chart was used.
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Low risk	"The scans were assessed blindly"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 196 participants who entered the study were analysed and accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Low risk	No other sources of bias were identified.

Turpie 1989

Methods

Study: RCT

Exclusions postrandomisation: 0

Losses to follow-up: 0

DVT diagnosis: FUT daily for 14 days or until discharge. Impedance plethysmography before study and day 3, 5, 7, 9, 11 and 14 days or on the day of discharge. If FUT or IPG was abnormal, phlebogram was carried out.

Follow-up: 14 days or until discharge (if earlier)

Statistical analysis: Fisher's exact or 1-sided Chi²

Participants

Country: USA

Total number of participants: 239

Total available for analysis: 239

Age: > 16 years

Sex: male and female

Inclusion criteria: all patients with head or spinal pathology including trauma

Turpie 1989 (Continued)

Exclusion criteria: history of iodine allergy, trauma to legs, mild head injury that needed only 24-hour surgery, those that needed anticoagulant treatment, or initial abnormal IPG

Interventions	Type of treatment: GCS thigh length (1 participant had knee length because of obesity) Control: 81 Treatment: 80 Duration: applied 12 hours before surgery, and removed after participant fully mobile (4 to 5 days later). Participants encouraged to mobilise early.
Outcomes	DVT (all) Control: 16 Treatment: 7 P = 0.023 Proximal DVT Control: 2 Treatment: 1 P not reported
Notes	Losses to follow-up: 1 unavailable for follow-up and 19 deaths during the follow-up period (none due to PE). It is not explicit if these participants were included in or excluded from the study. 1 participant developed PE. Source of funding not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	By "...a prescribed randomised arrangement"
Allocation concealment (selection bias)	Low risk	"Using sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	Low risk	"The results of the tests were interpreted independently by a panel of experts blinded to the patient's treatment group."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 236 participants accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcomes measures were reported.
Other bias	Low risk	No other sources of bias identified.

Wille-Jorgensen 1985

Methods	Study: RCT Exclusions postrandomisation: 20 Losses to follow-up: 0 DVT diagnosis: FUT preoperatively and on first, third, fifth, and seventh day postoperatively. Those who are FUT positive also had phlebography and perfusion lung scan.
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Wille-Jorgensen 1985 (Continued)

Follow-up: 7 days postoperatively for DVT, participants with suspected DVT also had V/Q scan at this time, follow-up for death at 30 days. 64 participants were observed for a median of 7 days due to early discharge (60), removing stockings early (2), or death (2).
Statistical analysis: Mann-Whitney U test

Participants	Country: Denmark Total number of participants: 196 Total available for analysis: 176 Age: > 39 years Sex: male and female Inclusion criteria: all patients for abdominal surgery Exclusion criteria: those with hepatic diseases with coagulation defects, anticoagulant treatment, PAD, and allergy to iodine
Interventions	Treatment: GCS thigh length Additional background thromboprophylaxis: UFH Control: 90 Treatment: 86 Duration: GCS were fitted on the day of surgery and continued for 7 days or until discharge.
Outcomes	DVT Control: 7 Treatment: 1 P < 0.05 PE Control: 6 Treatment: 2 P value: not significant (value not reported)
Notes	Heparin 5000 IU was given to all participants every 12 hourly for 7 days or until discharge. Thromboembolic complications are not clear. Incidence of proximal DVT not reported. No mention of adverse events Novo Diagnostics supplied heparin and thrombograph, and Kendall supplied the stockings.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"by random numbers"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	Low risk	"Phlebogram evaluated by radiologist not aware of the patient's treatment group" and scintigraphy "read blindly"
Incomplete outcome data (attrition bias) All outcomes	Low risk	20/196 participants withdrew, but all were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were addressed.

Wille-Jorgensen 1985 (Continued)

Other bias	Low risk	No other sources of bias identified.
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Wille-Jorgensen 1991

Methods	<p>Study: RCT Exclusions postrandomisation: 31 Losses to follow-up: 0 DVT diagnosis: FUT on the first, third, fifth, and seventh postoperative days and phlebography as indicated</p> <p>Follow-up: screened for DVT at 7 days, then monitored for death due to fatal PE at 30 days Statistical analysis: Kruskal–Wallis test, Chi² test, and Mantel–Haenszel test</p>
Participants	<p>Country: Denmark Total number of participants: 276 Total available for analysis: 245 Age: > 39</p> <p>Sex: male and female Inclusion criteria: all patients admitted for abdominal operations lasting over 1 hour Exclusion criteria: allergy to iodine, dextran. Severe peripheral vascular disease, pregnancy, GI bleeding</p>
Interventions	<p>Type of treatment: GCS length not stated. Additional background thromboprophylaxis: UFH Control: 81 Treatment: 79 Duration: worn until full mobilisation</p>
Outcomes	<p>DVT Control: 12 Treatment: 2 P < 0.013</p>
Notes	<p>On a background of heparin 5000 IU prophylaxis. 1 group received dextran and GCS, which we have excluded from our analysis.</p> <p>Incidence of proximal DVT was not reported.</p> <p>Participants were not routinely assessed for PE. 1 participant in the treatment group developed a fatal PE on the 14th postoperative day, however this participant had been excluded from the study on the second postoperative day due to poor compliance.</p> <p>Adverse events: bleeding complications, likely associated with heparin. No complications associated with the use of GCS were reported.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"continuous random numbers"
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used.

Wille-Jorgensen 1991 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	31 participants withdrew, but all were accounted for.
Selective reporting (reporting bias)	Low risk	Results of all outcome measures were reported.
Other bias	Unclear risk	Supported in part by grants from Novo A/S, Kabi Vitrum A/S, and The Kendall Company

BMI: body mass index

CVI: chronic venous insufficiency

DHE-LDH: dihydroergotamine + low-dose heparin

DVT: deep vein thrombosis

FUT: ¹²⁵I fibrinogen uptake test. A sustained difference of more than 20% between consecutive or opposite points or a raising count were considered diagnostic of DVT.

GCS: graduated compression stockings (also known as thrombo-embolic deterrent (TED) stockings). Compression is graduated, 18 mmHg, 14 mmHg, 8 mmHg, 10 mmHg, and 8 mmHg from ankle to upper thigh.

GI: gastrointestinal

IPC: intermittent pneumatic compression device

IPCC: intermittent pneumatic calf compression

IPG: impedance plethysmography

IU: international units

LMWH: low molecular weight heparin

NSAIDs: non-steroidal anti-inflammatory drugs

PAD: peripheral arterial disease

PE: pulmonary embolism

PVD: peripheral vascular disease

RCT: randomised controlled trial

UFH: unfractionated heparin

V/Q: ventilation/perfusion

VTE: venous thromboembolism

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ayhan 2013	Lacks appropriate control group. Compares the following groups of patients: low-pressure knee-length stockings, low-pressure thigh-length stockings, and moderate-pressure knee-length stockings
Barinov 2014	Lacks appropriate control arm. Compared low- vs moderate-pressure GCS, and knee-length vs thigh-length GCS
Belcaro 1993	Unclear whether participants were hospitalised, therefore study did not meet our inclusion criteria. Focused on patients with recurrent DVTs, including those with chronic DVT. Method of randomisation unclear. Reasons for dropouts unclear. The duration that stockings were worn is not mentioned. Method of monitoring the occurrence of DVT in the study is unclear.
Bolton 1978	Not randomised and not published as a paper. High-risk group of patients were involved (malignant diseases). A significant reduction in DVT was noted in the treatment group compared with the control group. The method of analysis seems appropriate.

Study	Reason for exclusion
Brunkwall 1991	Not published as a full paper. Abstract does not mention number of legs in each group (transplanted side versus non-transplanted side).
Caprini 1983	Control group is retrospective.
Chandhoke 1991	Lacks appropriate control group. Compares patients given warfarin (Coumadin) only to those given compression stockings only
CLOTS 2009	Included only stroke patients
Cohen 2007	Proximal asymptomatic DVT was diagnosed using venography, however it was unclear whether symptomatic DVT was also confirmed objectively using this method, and whether this was standardised throughout the study. It appears that some participants were scanned using ultrasound and some using venography. If this was the case, the split between the two methodologies is unclear. Furthermore, participants with asymptomatic DVT seem only to have been assessed proximally; it was unclear whether they were also examined for more distal DVTs. It was not clear which veins were examined for proximal DVTs and whether this was standardised throughout the study. We contacted the authors seeking clarification, however these queries remained unanswered at the time of publication.
Fasting 1985	Lacks appropriate control group. Compares patients given heparin only to those given compression stockings only
Flanc 1969	Thick elastic compression stockings used, not TED stockings. This study was randomised and would have been suitable for analysis.
Gao 2012	Lacks appropriate control group. 2 groups: GCS only versus GCS + intermittent pneumatic compression
Hansberry 1991	Lacks appropriate control group. 3 groups: thromboembolic stocking only versus external sequential pneumatic compression stockings only versus heparin + dihydroergotamine
Ibegbuna 1997	Incidence of DVT not assessed. Studies venous haemodynamics
Ido 1995	Haemodynamic study of mean blood flow velocity in participants wearing GCS versus those not wearing GCS. Incidence of GCS in these patient groups not reported.
KANT study	Lacks appropriate control group. Compares 3 groups: stockings only versus LMWH 7 days versus LMWH 14 days
Koopmann 1985	Lacks appropriate control group. Compares patients given heparin only to those given stockings only
Lacut 2005	Lacks appropriate control group. All participants wore elastic compression stockings (stockings only versus stockings + intermittent pneumatic compression).
Lee 1989	Lacks appropriate control group. Compares 3 groups: sodium heparin versus calcium heparin versus stockings
Lobastov 2013	Lacks appropriate control group. Compares the following 2 experimental groups: electrical calf stimulation + low-dose unfractionated heparin + elastic compression versus low-dose unfractionated heparin + elastic compression
Maksimovic 1996	Lacks appropriate control group. All participants wore stockings: GCS + standard heparin versus GCS + dipyridamole + acetylsalicylic acid versus GCS + placebo

Study	Reason for exclusion
Manella 1981	Incidence of DVT not assessed. Measures residual limb volume
Marston 1995	Lacks appropriate control group. All participants wore stockings. Compares LMWH + stockings versus stockings alone
Maxwell 2000	Lacks appropriate control group. Compares intermittent pneumatic compression stockings versus LMWH
Muir 2000	RCT based on stroke patients
NCT00333021	Lacks appropriate control group, based on reported clinical protocol. Formal methodology not published. No mention of use of mechanical method of thromboprophylaxis in this trial
NCT01234064	Substudy of Perioperative Ischemic Evaluation 2 (POISE-2) trial (evaluating efficacy of aspirin in preventing venous thromboembolism); results for GCS vs no GCS arms not published
NCT01935414	Lacks appropriate control group. Compared neuromuscular stimulation versus TED stockings
Necioglu 2008	Lacks appropriate control group. LMWH versus GCS
Norgren 1996	Compares patients wearing intermittent pneumatic compression stockings + GCS to patients on enoxaparin, rather than to a control group of patients wearing intermittent pneumatic compression stockings only
Nurmohamed 1996	All participants wore stockings. Compares patients wearing stockings and taking nadroparin to patients wearing stockings alone, rather than to a control group of patients not wearing stockings and on nadroparin as background prophylaxis
Orken 2009	Lacks appropriate control group. LMWH versus GCS
Patel 1988	Antithrombotic stockings, but does not state if compression graduated stockings. French paper
Perkins 1999	Difficult to analyse as not published as a full paper
Porteous 1989	This study compared above-knee stockings to below-knee stockings, rather than to a control group of no stockings or another method of prophylaxis.
Rabe 2013	This study aimed to assess the effectiveness of thigh-length vs lower-leg compression in preventing post-thrombotic syndrome in people known to have proximal DVT.
Ramos 1996	This study used pneumatic compression stockings rather than graduated compression stockings.
Rasmussen 1988	This study relied solely on the Tc ^{99m} plasmin test, which is associated with a high frequency of false positives. Diagnosis of DVT was not confirmed using another objective test. Furthermore, the method of randomisation used in this trial does not appear to be reliable, due to substantial difference in number of participants allocated to the GCS-only group (74 participants) and the GCS + heparin group (89 participants).
Rocca 2012	This study aimed to assess the effectiveness of 2 different types of stockings in the treatment and prevention of venous ulcers. Does not assess incidence of DVT
Rosengarten 1970	This trial used Tubigrip rather than graduated compression stockings.
Ryan 2002	This study compared 2 groups: mechanical compression + aspirin versus GCS + aspirin. Lacks a control group with participants on aspirin with no stockings

Study	Reason for exclusion
Sakon 2012	Lacks appropriate control group. Compares incidence of DVT in 2 groups: darexaban versus GCS
Serin 2010	Lacks appropriate control group. Compares incidence of DVT in 2 groups: LMWH versus GCS + IPC
Shilpa 2013	Lacks appropriate control group. Compared TED stockings versus crepe bandage
Silbersack 2004	This study compared 2 groups: LMWH + IPC versus LMWH + GCS. Lacks a control group of participants on LMWH with no stockings
Sobieraj-Teague 2012	Lacks appropriate control group. Compares incidence of DVT in 2 groups: GCS versus Venowave + GCS
Sultan 2011	This study compared the effectiveness of engineered compression stockings in the prevention of DVT following ankle fractures. We sought further information from trialists as results were only published as a conference abstract. Not all trial participants had been hospitalised, therefore the trial did not meet our inclusion criteria.
Sultan 2014	Lacks appropriate control group. Compared ankle injury stockings versus Tubigrip in participants with ankle fractures
Vignon 2013	Lacks appropriate control group. Compared the following 2 experimental groups: IPC + GCS versus GCS alone
Westrich 1996	This study used a pneumatic plantar compression device rather than graduated compression stockings.
Wilkins 1952	Based solely on clinical diagnosis of DVT instead of using Doppler/venography for confirmation, as set out in the criteria for this review
Wille-Jorgensen 1986	Lacks appropriate control group. Compared the following 2 experimental groups: heparin + GCS versus heparin + dihydroergotamine
Wilson 1994	Studies venous haemodynamics. Does not assess the incidence of DVT
Yang 2009	Lacks appropriate experimental groups. Compared the following 3 groups: IPC versus LMWH versus no thromboprophylaxis
Zhang 2011	Lacks appropriate experimental groups. Compared the following 2 groups: IPC versus no thromboprophylaxis
Zheng 2014	Lacks appropriate control group. Compared GCS + LMWH versus GCS alone

DVT: deep vein thrombosis

GCS: graduated compression stockings

IPC: intermittent pneumatic compression

LMWH: low molecular weight heparin

TED: thrombo-embolic deterrent

Characteristics of studies awaiting assessment *[ordered by study ID]*

[Celebi 2001](#)

Methods	Study: randomised controlled trial Losses to follow-up: 2 participants in control group died during treatment. DVT diagnosis: deep venous Doppler ultrasonography
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Celebi 2001 (Continued)

	PE diagnosis: pulmonary scintigraphy
Participants	Country: Turkey Total number of participants: 274 Total available for analysis: 274 Sex: male and female Inclusion criteria: patients undergoing major abdominal surgery
Interventions	Type of treatment: compression stockings Control: 91 (LMWH only) Treatment: 92 (LMWH and compression stockings) Duration: not specified in abstract
Outcomes	DVT Control: 8 Treatment: 3 P > 0.05 (not significant)
Notes	Turkish paper Low molecular weight heparin (nadroparin calcium 0.3 mL 2850 IU anti-factor Xa) was given to both control and treatment groups. This study included an additional group of patients who wore stockings but were not administered LMWH that is not relevant to this review. Awaiting translation

DVT: deep vein thrombosis

FUT: I¹²⁵ fibrinogen uptake test

GCS: graduated compression stockings

LMWH: low molecular weight heparin

PE: pulmonary embolism

Characteristics of ongoing studies [ordered by study ID]

ChiCTR1800014257

Trial name or title	The strategies of risk-stratified prophylaxis of deep venous thrombosis after gynaecologic pelvic surgery in patients at different levels of risk: a prospective multicenter randomised controlled trial
Methods	Multicentre RCT
Participants	Inclusion criteria <ul style="list-style-type: none"> aged ≥ 50 years hypertension varicose vein of lower extremity pelvic laparotomy expected surgery time ≥ 1 h postsurgery bedridden time ≥ 48 h Patients are risk stratified into high- (at least 2 criteria met) and very high-risk groups (3 or more criteria met).
Interventions	4 arms based on risk of DVT: <ul style="list-style-type: none"> GCS only (high-risk group, n = 404) GCS + LMWH (high-risk group, n = 404)

Graduated compression stockings for prevention of deep vein thrombosis (Review)

ChiCTR1800014257 (Continued)

- GCS + IPC (very high-risk group, n = 102)
- GCS + LMWH + IPC (very high-risk group, n = 102)

Outcomes	Primary outcome: DVT diagnosed using colour Doppler ultrasound
Starting date	1 January 2018
Contact information	Zhengyu Zhang 8 Gongti Road South, Chaoyang District, Beijing, China Telephone: +86 13801237287 Email: zhangzhenyu@coga.org.cn
Notes	Trial information from www.chictr.org.cn/showproj.aspx?proj=24115 Trial end date: 31 December 2020

GAPS

Trial name or title	Graduated compression as an Adjunct to Pharmacoprophylaxis in Surgery (GAPS). Examining the benefit of GCS as an adjunct to low dose LMWH in the prevention of VTE in elective surgical inpatients identified as moderate or high risk for VTE
Methods	Multicentre RCT
Participants	Elective surgical inpatients assessed as being at moderate or high risk of VTE Planned sample size: 2236
Interventions	2 arms: GCS only vs GCS + LMWH
Outcomes	Primary outcome: VTE within 90 days (composite endpoint of duplex ultrasound-proven new lower-limb DVT up to 90 days postsurgery (symptomatic or asymptomatic) and symptomatic PE (imaging confirmed) up to 90 days postsurgery)
Starting date	1 May 2016
Contact information	Professor Alun Davies Section of Vascular Surgery, Room 3E, 4th Floor East Wing, Charing Cross Hospital, Fulham Palace Road, London W6 8RF. Telephone: 0208 8467 320 Email: a.h.davies@imperial.ac.uk
Notes	ISRCTN: 13911492 Trial website: w3.abdn.ac.uk/hsru/gaps/ Overall trial end date: 30 November 2019

IRCT2017080935594N1

Trial name or title	Comparison of efficacy compressive stocking with heparin and enoxaparin in prevention of deep vein thrombosis of lower extremities in hysterectomized patients
Methods	Randomised trial
Participants	Women under 60 years old undergoing hysterectomy for indications other than malignancy
Interventions	Participants were randomised to 1 of 4 groups: <ul style="list-style-type: none"> • heparin subcutaneously 5000 units every 12 hours for 3 days plus compressive socks; • heparin without compressive socks; • prophylaxis with subcutaneous enoxaparin 40 mg daily for 3 days plus compressive socks; • enoxaparin without compressive socks.
Outcomes	The presence or absence of thrombosis on Doppler ultrasonography of the deep veins of the lower limb at 2 weeks follow-up
Starting date	23 August 2017
Contact information	Ahmad Enhesari Kerman University of Medical Sciences Afzalipour Pardis, Early axis of seven Alavi Gardens, Kerman, Iran 7916913555 Telephone: +98 34 3132 5700 Fax: +98 31325605 Email: Enhesari@Kmu.ac.ir Web address: www.kmu.ac.ir/
Notes	Trial information from en.irct.ir/trial/26850 Expected recruitment end date: 23 August 2018

DVT: deep vein thrombosis

GCS: graduated compression stockings

IPC: intermittent pneumatic compression

LMWH: low molecular weight heparin

RCT: randomised controlled trial

VTE: venous thromboembolism

DATA AND ANALYSES

Comparison 1. Incidence of DVT with stockings and without stockings

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All specialties	20	2853	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.43]
1.1 General surgery	10	1486	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.30 [0.22, 0.41]
1.2 Orthopaedic surgery	6	598	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.47 [0.32, 0.68]

Graduated compression stockings for prevention of deep vein thrombosis (Review)

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 Other specialties	4	769	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.28 [0.16, 0.48]
2 All specialties - surgical vs medical	20	2853	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.43]
2.1 Surgery	19	2693	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.44]
2.2 Medicine	1	160	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.03, 0.51]

Analysis 1.1. Comparison 1 Incidence of DVT with stockings and without stockings, Outcome 1 All specialties.

Analysis 1.2. Comparison 1 Incidence of DVT with stockings and without stockings, Outcome 2 All specialties - surgical vs medical.

Comparison 2. Incidence of proximal DVT with stockings and without stockings

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All specialties	8	1035	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.26 [0.13, 0.53]
1.1 General surgery	2	316	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.14 [0.00, 6.82]
1.2 Orthopaedic surgery	4	398	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.25 [0.12, 0.53]
1.3 Other specialties	2	321	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.52 [0.05, 5.03]
2 All specialties - surgical vs medical	8	1035	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.26 [0.13, 0.53]
2.1 Surgery	7	875	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.26 [0.13, 0.53]
2.2 Medicine	1	160	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Incidence of proximal DVT with stockings and without stockings, Outcome 1 All specialties.

Analysis 2.2. Comparison 2 Incidence of proximal DVT with stockings and without stockings, Outcome 2 All specialties - surgical vs medical.

Comparison 3. Incidence of PE with stockings and without stockings

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All specialties	5	569	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.38 [0.15, 0.96]
1.1 General surgery	2	271	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.33 [0.09, 1.24]
1.2 Orthopaedic surgery	3	298	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.44 [0.12, 1.58]
1.3 Other specialties	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 All specialties - surgical vs medical	5	569	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.38 [0.15, 0.96]
2.1 Surgery	5	569	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.38 [0.15, 0.96]
2.2 Medicine	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 3.1. Comparison 3 Incidence of PE with stockings and without stockings, Outcome 1 All specialties.

Analysis 3.2. Comparison 3 Incidence of PE with stockings and without stockings, Outcome 2 All specialties - surgical vs medical.

Comparison 4. Sensitivity analysis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Method of randomisation	20	2853	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.43]
1.1 Method of randomisation inappropriate or not reported	12	1565	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.34 [0.25, 0.45]
1.2 Appropriate method of randomisation	8	1288	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.26, 0.50]
2 Unit of analysis for randomisation	20	2853	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.43]
2.1 Individual participants	13	1681	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.38 [0.29, 0.49]
2.2 Individual legs	7	1172	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.28 [0.19, 0.42]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Use of background method of thromboprophylaxis	20	2853	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.43]
3.1 Trials without background thromboprophylaxis	9	1497	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.38 [0.29, 0.50]
3.2 Trials with background thromboprophylaxis	11	1356	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.29 [0.20, 0.42]
4 Method of diagnosis	20	2853	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.35 [0.28, 0.43]
4.1 Fibrinogen uptake test alone	8	1209	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.31 [0.22, 0.44]
4.2 Fibrinogen uptake test and phlebography	6	1013	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.29 [0.19, 0.43]
4.3 Ultrasonography	2	238	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.48 [0.25, 0.94]
4.4 Phlebography	4	393	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.47 [0.29, 0.75]

Analysis 4.1. Comparison 4 Sensitivity analysis, Outcome 1 Method of randomisation.

Analysis 4.2. Comparison 4 Sensitivity analysis, Outcome 2 Unit of analysis for randomisation.

Analysis 4.3. Comparison 4 Sensitivity analysis, Outcome 3 Use of background method of thromboprophylaxis.

Study or subgroup	Stockings n/N	No stockings n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Heterogeneity: $\tau^2=0$; $\chi^2=21.07$, $df=19$ ($P=0.33$); $I^2=9.83\%$					
Test for overall effect: $Z=9.49$ ($P<0.0001$)					
Test for subgroup differences: $\chi^2=1.35$, $df=1$ ($P=0.25$), $I^2=25.97\%$					
Favours Stockings 0.002 0.1 1 10 500 Favours No stockings					

Analysis 4.4. Comparison 4 Sensitivity analysis, Outcome 4 Method of diagnosis.

Study or subgroup	Stockings n/N	No stockings n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
4.4.1 Fibrinogen uptake test alone					
Holford 1976	11/48	23/47		6.9%	0.33[0.14,0.75]
Scurr 1977	8/70	28/70		8.42%	0.23[0.11,0.48]
Torngren 1980	4/98	12/98		4.62%	0.34[0.12,0.94]
Ohlund 1983	7/31	15/31		4.51%	0.33[0.12,0.93]
Bergqvist 1984	0/80	8/80		2.39%	0.12[0.03,0.51]
Turner 1984	0/104	4/92		1.23%	0.11[0.02,0.83]
Shirai 1985	5/126	17/126		6.3%	0.3[0.13,0.73]
Mellbring 1986	8/54	8/54		4.3%	1[0.35,2.88]
Subtotal (95% CI)	611	598		38.66%	0.31[0.22,0.44]
Total events: 43 (Stockings), 115 (No stockings)					
Heterogeneity: $\tau^2=0$; $\chi^2=8.03$, $df=7$ ($P=0.33$); $I^2=12.79\%$					
Test for overall effect: $Z=6.53$ ($P<0.0001$)					
4.4.2 Fibrinogen uptake test and phlebography					
Allan 1983	15/97	37/103		12.08%	0.35[0.18,0.65]
Wille-Jorgensen 1985	1/86	7/90		2.4%	0.22[0.05,0.9]
Scurr 1987	1/78	7/78		2.39%	0.21[0.05,0.86]
Turpie 1989	7/80	16/81		6.2%	0.41[0.17,0.99]
Wille-Jorgensen 1991	2/79	12/81		4.02%	0.22[0.07,0.65]
Kierkegaard 1993	0/80	8/80		2.39%	0.12[0.03,0.51]
Subtotal (95% CI)	500	513		29.48%	0.29[0.19,0.43]
Total events: 26 (Stockings), 87 (No stockings)					
Heterogeneity: $\tau^2=0$; $\chi^2=2.93$, $df=5$ ($P=0.71$); $I^2=0\%$					
Test for overall effect: $Z=6.07$ ($P<0.0001$)					
4.4.3 Ultrasonography					
Barnes 1978	0/8	5/10		1.18%	0.1[0.01,0.71]
Chin 2009	14/110	22/110		9.46%	0.59[0.29,1.2]
Subtotal (95% CI)	118	120		10.64%	0.48[0.25,0.94]
Total events: 14 (Stockings), 27 (No stockings)					
Heterogeneity: $\tau^2=0$; $\chi^2=2.79$, $df=1$ ($P=0.09$); $I^2=64.22\%$					
Test for overall effect: $Z=2.13$ ($P=0.03$)					
4.4.4 Phlebography					
Tsapogas 1971	2/51	6/44		2.3%	0.29[0.07,1.22]
Fredin 1989	3/49	13/47		4.21%	0.22[0.07,0.63]
Kalodiki 1996	8/32	12/32		4.37%	0.56[0.2,1.61]
Hui 1996	38/84	30/54		10.35%	0.66[0.34,1.31]
Subtotal (95% CI)	216	177		21.23%	0.47[0.29,0.75]
Favours Stockings 0.01 0.1 1 10 100 Favours No stockings

APPENDICES

Appendix 1. CENTRAL search strategy March 2017

#1	MESH DESCRIPTOR Venous Thrombosis EXPLODE ALL TREES	2041
#2	MESH DESCRIPTOR Thromboembolism EXPLODE ALL TREES	1433
#3	MESH DESCRIPTOR Thrombosis	1267
#4	thrombo*:TI,AB,KY	31059
#5	thrombu*:TI,AB,KY	1336
#6	embol*:TI,AB,KY	5962
#7	(dvt* or PE or VTE):TI,AB,KY	4996
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	37392
#9	MESH DESCRIPTOR Stockings, Compression	165
#10	MESH DESCRIPTOR Compression Bandages	99
#11	(stocking* or hosiery* or tights* or sock* or bandage* or compres*):TI,AB,KY	8388
#12	(VenoTrain* or Ulcertec or SurePress* or ComfortPro or Comfort-Pro or "Ulcer Kit" or Sigvaris):TI,AB,KY	23
#13	#9 OR #10 OR #11 OR #12	8388
#14	#8 AND #13	1023
#15	* NOT SR-PVD:CC AND 31/03/2014 TO 31/03/2017:DL	272119
#16	#14 AND #15	238

Appendix 2. Trials registry searches March 2017

ClinicalTrials.gov

147 studies found for: compression AND (thrombosis OR embolism OR DVT OR PE)

World Health Organization International Clinical Trials Registry Platform

30 records for 30 trials; compression or stockings in Title and (thrombosis OR embolism OR DVT OR PE) in Condition

27 records for 27 trials; (thrombosis OR embolism OR DVT OR PE) in Condition AND (compression or stockings) Intervention

ISRCTN Register

24 results compression stockings

Appendix 3. Database searches June 2018

Source	Search strategy	Hits retrieved
1. VASCULAR REGISTER IN CRSW	Stocking AND DVT AND 2017 OR 2018	0
2. CENTRAL	#1 MESH DESCRIPTOR Venous Thrombosis EXPLODE ALL TREES 2377 #2 MESH DESCRIPTOR Thromboembolism EXPLODE ALL TREES 1748 #3 MESH DESCRIPTOR Thrombosis 1618 #4 thrombo*:TI,AB,KY 37896 #5 thrombu*:TI,AB,KY 1701 #6 embol*:TI,AB,KY 7568 #7 (dvt* or PE or VTE):TI,AB,KY 6320 #8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 45955 #9 MESH DESCRIPTOR Stockings, Compression 188 #10 MESH DESCRIPTOR Compression Bandages 123 #11 (stocking* or hosiery* or tights* or sock* or bandage* or com- pres*):TI,AB,KY 10338 #12 (VenoTrain* or Ulcertec or SurePress* or ComfortPro or Comfort-Pro or "Ulcer Kit" or Sigvaris):TI,AB,KY 25 #13 #9 OR #10 OR #11 OR #12 10338 #14 #8 AND #13 1202 #15 01/01/2017 TO 11/06/2018:CD 285491 #16 #14 AND #15 235	235
3. ClinicalTrials.gov	compression thrombosis OR embolism OR DVT OR PE0 Start date on or after 01/01/2017 Last update posted on or before 06/12/2018	22
4. ICTRP Search Portal	compression or stockings in Title and (thrombosis OR embolism OR DVT OR PE)	41 50

(Continued)

(thrombosis OR embolism OR DVT OR PE) in Condition AND (compression or stockings) Intervention

5. MEDLINE (2017 AND 2018 ONLY)	1 exp Venous Thrombosis/ 51417	120
	2 exp THROMBOEMBOLISM/ 51479	
	3 THROMBOSIS/ 65664	
	4 thrombo*.ti,ab. 328580	
	5 thrombu*.ti,ab. 34506	
	6 embol*.ti,ab. 116862	
	7 (dvt* or PE or VTE).ti,ab. 47049	
	8 or/1-7 503827	
	9 Stockings, Compression/ 1337	
	10 Compression Bandages/ 779	
	11 (stocking* or hosiery* or tights* or sock* or bandage* or compres*).ti,ab. 153878	
	12 (VenoTrain* or Ulcertec or SurePress* or ComfortPro or Comfort-Pro or "Ulcer Kit" or Sigvaris).ti,ab. 30	
	13 or/9-12 154511	
	14 8 and 13 8944	
	15 randomized controlled trial.pt. 463544	
	16 controlled clinical trial.pt. 92478	
	17 randomized.ab. 414978	
	18 placebo.ab. 189985	
	19 drug therapy.fs. 2026770	
	20 randomly.ab. 292442	
	21 trial.ab. 431981	
	22 groups.ab. 1807008	
	23 or/15-22 4228218	
	24 exp animals/ not humans.sh. 4470062	
	25 23 not 24 3655192	
	26 14 and 25 1938	
	27 (2017* or 2018*).ed. 1410268	
	28 26 and 27 120	
6. Embase (2017 AND 2018 ONLY)	1 exp vein thrombosis/ 117897	483
	2 exp thromboembolism/ 447229	
	3 thrombosis/ 124510	

(Continued)

- 4 thrombo*.ti,ab. 468161
- 5 thrombu*.ti,ab. 51801
- 6 embol*.ti,ab. 166543
- 7 (dvt* or PE or VTE).ti,ab. 75124
- 8 or/1-7 801765
- 9 compression stocking/ 2205
- 10 compression bandage/ 2132
- 11 (stocking* or hosiery* or tights* or sock* or bandage* or compres*).ti,ab. 188533
- 12 (VenoTrain* or Ulcertec or SurePress* or ComfortPro or Comfort-Pro or "Ulcer Kit" or Sigvaris).ti,ab. 62
- 13 or/9-12 190524
- 14 8 and 13 14787
- 15 randomized controlled trial/ 505723
- 16 controlled clinical trial/ 460951
- 17 random\$.ti,ab. 1309942
- 18 randomization/ 78407
- 19 intermethod comparison/ 235704
- 20 placebo.ti,ab. 273502
- 21 (compare or compared or comparison).ti. 470023
- 22 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 1753437
- 23 (open adj label).ti,ab. 64566
- 24 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 209146
- 25 double blind procedure/ 150639
- 26 parallel group\$1.ti,ab. 21829
- 27 (crossover or cross over).ti,ab. 93000
- 28 ((assign\$ or match or matched or allocation) adj5 (alternate or group\$1 or intervention\$1 or patient\$1 or subject\$1 or participant\$1)).ti,ab. 283079
- 29 (assigned or allocated).ti,ab. 332145
- 30 (controlled adj7 (study or design or trial)).ti,ab. 295234
- 31 (volunteer or volunteers).ti,ab. 224581
- 32 trial.ti. 251314
- 33 or/15-32 4039780
- 34 14 and 33 2822

(Continued)

35 (2017* or 2018*).em. 3562214

36 34 and 35 483

37 from 36 keep 1-483 483

7. CINAHL (2017 AND 2018 ONLY)	S31 S29 AND S30 18 S30 EM 2017 OR EM 2018 361,822 S29 S14 AND S28 425 S28 S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 341,275 S27 MH "Random Assignment" 38,519 S26 MH "Triple-Blind Studies" 85 S25 MH "Double-Blind Studies" 24,789 S24 MH "Single-Blind Studies" 7,975 S23 MH "Factorial Design" 919 S22 MH "Placebos" 8,349 S21 MH "Clinical Trials" 93,065 S20 TX "multi-centre study" OR "multi-center study" OR "multicentre study" OR "multicenter study" OR "multi-site study" 4,466 S19 TX crossover OR "cross-over" 14,523 S18 AB placebo* 28,225 S17 TX random* 218,477 S16 TX trial* 249,805 S15 TX "latin square" 142 S14 S8 AND S13 1,660 S13 S9 OR S10 OR S11 OR S12 25,775 S12 TX VenoTrain* or Ulcertec or SurePress* or ComfortPro or Comfort-Pro or "Ulcer Kit" or Sigvaris 13 S11 TX stocking* or hosiery* or tights* or sock* or bandage* or compres* 25,772 S10 (MH "Elastic Bandages") 112 S9 (MH "Compression Garments") 1,652 S8 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 56,491 S7 TX dvt* or PE or VTE 11,032 S6 TX embol* 15,079 S5 TX thrombu* 2,453 S4 TX thrombo* 39,098 S3 (MH "Thrombosis") 4,634	18
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(Continued)

S2 (MH "Thromboembolism+") 7,488

S1 (MH "Venous Thrombosis+") 6,387

8. AMED (2017 AND 2018 ONLY)	1 exp THROMBOEMBOLISM/ 72	1
	2 THROMBOSIS/ 199	
	3 thrombo*.ti,ab. 740	
	4 thrombu*.ti,ab. 39	
	5 embol*.ti,ab. 226	
	6 (dvt* or PE or VTE).ti,ab. 246	
	7 or/1-6 1064	
	8 Bandages/ 427	
	9 (stocking* or hosiery* or tights* or sock* or bandage* or compres*).ti,ab. 2606	
	10 (VenoTrain* or Ulcertec or SurePress* or ComfortPro or Comfort-Pro or "Ulcer Kit" or Sigvaris).ti,ab. 0	
	11 or/8-10 2914	
	12 7 and 11 52	
	13 ("2017" or "2018").yr. 2075	
	14 12 and 13 1	
	15 from 14 keep 1 1	

FEEDBACK

Excluded studies, 14 September 2015

Summary

This study excludes for inadequate reason the two most recent, largest and relevant studies on this topic ([CLOTS 2009](#); [Cohen 2007](#)). Both studies showed no benefit to stockings and if included within the review would have meant the conclusions would be changes completely to showing no conclusive benefit of stockings. Most of the included studies are old, small patients numbers and only presented asymptomatic thrombosis events. All of questionable relevance to current practice. Given these studies showing no benefit of stocking and potential for harm I feel the Cochrane review is inaccurate and should not be allowed and if it cannot be immediately updated to included these studies the review should be withdrawn.

Reply

Mr Parker highlights the exclusion of two trials from this Cochrane review ([CLOTS 2009](#) and [Cohen 2007](#)), stating "inadequate reason" for their exclusion. The reasons for excluding both these trials are clearly stated in our review, and revisited below.

The [CLOTS 2009](#) trial was excluded as it focused on patients hospitalised following acute stroke. The authors of this trial have clearly stated that a potential mechanism of action of GCS (i.e. increasing velocity of venous blood flow by improving effectiveness of the calf muscle pump) is lost in patients with severe leg weakness following acute stroke. This patient group, and consequently the CLOTS trial, has therefore been excluded from our review, and is the focus of a separate Cochrane review exclusively focusing on stroke patients ([Naccarato 2010](#)).

The [Cohen 2007](#) study was excluded following thorough critical review, as it was unclear whether a standardized protocol was used throughout the study. We noted a number of discrepancies in this trial (such as variation in the use of imaging modalities and how an "objective" diagnosis of symptomatic DVTs was made), and felt it was unclear whether all patients or only selected patients were routinely scanned for DVT. This placed this study at high risk of bias due to lack of consistency in outcome measurement, and it was therefore

excluded from this review. With regards to adverse events, 7 of 391 patients (2%) in the Cohen study were stated to have experienced an adverse event related to the wearing of stockings. However, the nature or severity of these events was not reported. Overall, frequency of adverse events was comparable in the fondaparinux-only and fondaparinux+GCS groups. We attempted to contact the authors of this trial to seek further clarification and received no response. Nevertheless, despite the high potential risk for bias associated with this study, its inclusion would not have changed the overall findings on meta-analyses.

Though a number of studies included in this review had small numbers, our conclusions are based upon meta-analyses of 2745 analytic units, making our findings robust and reliable.

In conclusion we see no reason to change the findings of our review.

Contributors

Feedback: Martyn Parker

MP: I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

Response: Ashwin Sachdeva, Timothy Lees

WHAT'S NEW

Date	Event	Description
17 April 2019	Amended	Errors in 'anticipated absolute effects' in Summary of Findings tables corrected.

HISTORY

Protocol first published: Issue 2, 1999

Review first published: Issue 3, 2000

Date	Event	Description
12 June 2018	New search has been performed	Searches re-run. One previously excluded study now included. Six new studies excluded. Three new ongoing studies identified.
12 June 2018	New citation required but conclusions have not changed	Searches re-run. One previously excluded study now included. Six new studies excluded. Three new ongoing studies identified. Text amended to reflect current standards. 'Summary of findings' table added. Conclusions not changed.
28 October 2015	Feedback has been incorporated	Feedback and review authors' response to feedback added.
5 April 2014	New search has been performed	Searches re-run. One additional trial included. Twenty-three new studies excluded.
5 April 2014	New citation required but conclusions have not changed	Searches re-run. One additional trial included. Twenty-three new studies excluded. Trials assessing the effectiveness of stockings and those assessing the effectiveness of stockings over a background method of thromboprophylaxis were merged in the analysis. Text updated. No changes to conclusions.
10 May 2010	New citation required but conclusions have not changed	Two new authors updated the review.
15 March 2010	New search has been performed	The review was updated, and two included studies added. Thirty-five excluded studies added.

Date	Event	Description
8 September 2008	Amended	Converted to new review format.
15 February 2008	Feedback has been incorporated	An interim response added to feedback to say that the review is in the process of being updated. The authors intend to address the comments and provide a full response with the update.
26 November 2003	New search has been performed	Four excluded studies added.

CONTRIBUTIONS OF AUTHORS

AS: evaluated trials for inclusion; assessed quality of trials; extracted data; updated review

MD: evaluated trials for inclusion; cross-checked and authenticated data extraction; assessed quality of trials; updated review

TL: re-checked and authenticated the selected trials for inclusion; checked the updated review

DECLARATIONS OF INTEREST

AS: has declared that travel and accommodation expenses were covered by the conference organisers to present the findings of the 2014 version of this review at the 21st European Vascular Course in Maastricht. He has also previously received funding from the following organisations for an unrelated project: National Institute for Health Research, Cancer Research UK, The Urology Foundation, Rosetrees Trust, and JGW Patterson Foundation.

MD: none known

TL: has declared that he is entitled to royalties from *Venous Disease Simplified*, which are donated to charity. He receives expenses for travel between places of work as part of his normal job and has no known conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We excluded two trials including stroke patients, [CLOTS 2009](#); [Muir 2000](#), from this review as they are the subject of another review undertaken by Cochrane Stroke ([Naccarato 2010](#)).

Previous versions of this review divided trials into two groups: graduated compression stockings (GCS) as sole method of thromboprophylaxis (i.e. those that compared GCS alone versus no thromboprophylaxis) and GCS as adjuvant method of thromboprophylaxis (i.e. those that compared GCS over a background method of thromboprophylaxis versus background method of thromboprophylaxis alone). Since both these groups of trials test the same treatment effect (i.e. with stockings versus without stockings), we merged all trials in the 2014 update to increase the power of the review.

Since proximal deep vein thrombosis is associated with an increased risk of pulmonary embolism and death ([Seinturier 2005](#)), we specifically reported incidence of proximal deep vein thrombosis and pulmonary embolism amongst the included studies (where available).

In keeping with Cochrane's recommendations, we have reassessed studies previously classified as excluded studies for reasons including 'not randomised' as not relevant for this updated version and have removed them from the review. We have reassessed one previously excluded study as an included study.

INDEX TERMS**Medical Subject Headings (MeSH)**

*Stockings, Compression; Hospitalization; Orthopedic Procedures; Postoperative Complications [*prevention & control]; Pulmonary Embolism [*prevention & control]; Randomized Controlled Trials as Topic; Surgical Procedures, Operative; Venous Thrombosis [*prevention & control]

MeSH check words

Humans