# 39 Vascular surgery

## 39.1 Introduction

This section covers patients undergoing vascular surgery. Vascular surgery is a surgical specialty dealing specifically with disorders of the arteries, veins and lymphatics around the body excluding the heart and brain. It also includes dealing with the consequences of vascular disease, such as limb amputation. Procedures range from these which can be long and involve interruption of flow in vessels and reduce patient mobility, to those which are more minor and can be done as day cases such as varicose veins surgery. High doses of anticoagulation are often given as part of the surgical procedure on more major cases.

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and its complication, pulmonary embolism (PE), is a common cause of morbidity and mortality after vascular surgery unless prophylaxis is given. However there are often also high risks of bleeding. There is a need to identify how to best reduce this risk of VTE using mechanical or pharmacological prophylaxis.

Factors that may alter the risk of VTE:

- Arterial surgery patients are often elderly and immobile.
- Many arterial surgery patients will already be receiving antiplatelet therapy and some will be on warfarin or other anticoagulants.
- Systemic heparin is frequently administered during surgery for arterial disease.
- Surgery for varicose veins is mostly in women; oral contraceptive use and hormone replacement therapy are therefore more commonly associated with varicose veins surgery.

Factors that increase the risk of bleeding or hazard associated with it:

- Patients using anticoagulation or antiplatelet therapy not related to surgery will have an increased risk of bleeding.

Other factors that may alter the choice of prophylaxis:

- The use of intermittent compression devices is contraindicated in patients with peripheral arterial disease.
- The use of intermittent compression devices and anti-embolism/graduated compression stockings will usually be inappropriate on the operated leg for a patient undergoing lower limb arterial surgery.
- Anti-embolism/graduated compression stockings will be contraindicated for patients with lower limb arterial disease.

## 39.2 Review question: What is the effectiveness of different pharmacological and mechanical prophylaxis strategies (alone or in combination) for people undergoing vascular surgery?

**Table 224: PICO characteristics of review question**

| | |
|---|---|
| **Population** | Adults and young people (16 years and older) undergoing vascular surgery who are admitted to and discharged from hospital |
| **Interventions** | Mechanical:<br>• Anti-embolism stockings (AES) (above or below knee)<br>• Intermittent pneumatic compression (IPCD) devices (full leg or below knee)<br>• Foot pumps or foot impulse devices (FID) |

| | |
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| | • Electrical stimulation (including Geko devices)<br>• Continuous passive motion<br><br>Pharmacological:<br>• Unfractionated heparin (UFH) (low dose, administered subcutaneously)<br>• Low molecular weight heparin (LMWH), licensed in UK:<br>  ○ enoxaparin (standard prophylactic dose 40mg daily; minimum 20mg daily* to maximum 60mg twice daily*)<br>  ○ dalteparin (standard prophylactic dose 5000 units once daily; minimum 1250 units once daily* to maximum 5000 units twice daily*; obese patients – maximum 7500 twice units daily*)<br>  ○ tinzaparin (standard prophylactic dose 4500 units once daily; minimum 2500 units once daily* to maximum 4500 units twice daily*; obese patients – maximum 6750 twice daily*)<br>• LMWH, licensed in countries other than UK:<br>  ○ Bemiparin (standard 2500 units daily; minimum 2500 units daily to maximum 3500 units daily)<br>  ○ Certoparin (3000 units daily)<br>  ○ Nadroparin (standard 2850 units once daily; minimum 2850 units once daily to maximum up to 57 units/kg once daily)<br>  ○ Parnaparin (standard 3200 units once daily; minimum 3200 units once daily to maximum 4250 units once daily)<br>  ○ Reviparin (minimum 1750 units once daily to maximum 4200 units once daily)<br>• Vitamin K Antagonists:<br>  ○ warfarin (variable dose only)<br>  ○ acenocoumarol (all doses)<br>  ○ phenindione (all doses)<br>• Fondaparinux (all doses)*<br>• Apixaban (all doses)*<br>• Dabigatran (all doses)*<br>• Rivaroxaban (all doses)*<br>• Aspirin (up to 300mg)*<br><br>*off-label |
| **Comparison(s)** | Compared to:<br>• Other VTE prophylaxis treatment, including monotherapy and combination treatments (between class comparisons for pharmacological treatments only)<br>• No VTE prophylaxis treatment (no treatment, usual care, placebo)<br><br>Within intervention (including same drug) comparisons, including:<br>• Above versus below knee stockings<br>• Full leg versus below knee IPC devices<br>• Standard versus extended duration prophylaxis.<br>• Low versus high dose for LMWH<br>• Preoperative versus post-operative initiation of LMWH |
| **Outcomes** | Critical outcomes:<br>• All-cause mortality (up to 90 days from hospital discharge)<br>• Deep vein thrombosis (symptomatic and asymptomatic) (up to 90 days from hospital discharge). Confirmed by: radioiodine fibrinogen uptake test; venography; Duplex (Doppler) ultrasound; MRI; Impedance Plethysmography (used as rule out tool)<br>• Pulmonary embolism (symptomatic and asymptomatic) (up to 90 days from hospital |

| | |
|---|---|
| | discharge). Confirmed by: CT scan with spiral or contrast; pulmonary angiogram; ventilation/ perfusion scan including VQSpect; autopsy; echocardiography; clinical diagnosis with the presence of proven VTE<br>• Major bleeding (up to 45 days from hospital discharge). A major bleeding event meets one or more of the following criteria: results in death; occurs at a critical site (intracranial, intraspinal, pericardial, intraocular, retroperitoneal); results in the need for a transfusion of at least 2 units of blood ; leads to a drop in haemoglobin of ≥2g/dl; a serious or life threatening clinical event. Includes unplanned visit to theatre for control of bleeding<br>• Fatal PE (up to 90 days from hospital discharge). Confirmed by: CT scan with spiral or contrast; pulmonary angiogram; ventilation/ perfusion scan including VQSpect; autopsy; echocardiography; clinical diagnosis with the presence of proven VTE<br><br>Important outcomes:<br>• Clinically relevant non-major bleeding (up to 45 days from hospital discharge): bleeding that does not meet the criteria for major bleed but requires medical attention and/or a change in antithrombotic therapy.<br>• Health-related quality of life (validated scores only)(up to 90 days from hospital discharge)<br>• Heparin-induced thrombocytopaenia (HIT) (duration of study)<br>• Technical complications of mechanical interventions (duration of study) |
| **Study design** | Randomised controlled trials (RCTs), systematic reviews of RCTs. |
| **Strata** | Open vascular surgery (major aortic/leg bypass)<br>Varicose veins<br>Lower limb amputation |

## 39.3 Clinical evidence

A search was conducted for randomised trials comparing the effectiveness of mechanical and pharmacological prophylaxis strategies (alone or in combination) in people undergoing vascular surgery.

Eight RCTs reporting at least one of the three main outcomes were identified. Four studies were identified from the search[13 ,265 ,306 ,325] and five studies were included from the previous guideline CG92[20 ,91 190 ,275]. One of the studies included in CG92 was excluded (Killewich 1997[164]) as the length of follow up does not match the review protocol. Of the studies included from CG92, data for two studies [20 ,275] were extracted from a systematic review[61]. Evidence from all the studies is summarised in the clinical evidence summary below (Table 225). See also the study selection flow chart in appendix E, forest plots in Appendix L, study evidence tables in appendix H (details of the systematic review are also reported in appendix H), GRADE tables in appendix K and excluded studies list in appendix N.

**Table 225: Summary of studies included in the review**

| Study | Intervention and comparison | Population | Outcomes | Comments |
|---|---|---|---|---|
| **Strata: overall (not specified)** | | | | |
| Belch 1980[20] | Intervention (n = 24):<br>UFH, 2,500UI pre-operatively then 5,000UI 2x daily for 7 days, administered subcutaneously | n=49<br><br>People undergoing elective aortic bifurcation graft surgery | DVT (timepoint not reported): confirmed by radiolabelled fibrinogen or scanning | The trial was terminated because of excess bleeding complications in patients receiving subcutaneous |

| Study | Intervention and comparison | Population | Outcomes | Comments |
|---|---|---|---|---|
| | Comparison (n= 25)<br>Placebo, saline injections<br><br>Concomitant treatment:<br>All people received a routine dose of intravenous sodium heparin intra-operatively. | UK<br><br>No further details reported | PE (timepoint not reported): no definition reported<br><br>Major bleeding (timepoint not reported): no definition reported | heparin<br><br>Data extracted from systematic review (Collins 1988 [61]) |
| Farkas 1993[91] | Intervention (n = 122):<br>LMWH (Enoxaparin), 2100IU pre-op (standard dose), 4200IU post-op (high dose). Timing: Begun day pre-op and repeatedly daily until 7th day post- op<br><br>Comparison (n=111):<br>UFH 5000UI pre-op, 7500UI post-op. Timing: Begun day pre-op and repeated twice daily until 7th day post-op<br><br>Concomitant treatment: Intraoperative use of UFH (94.4%) or protamine (7.9%) was authorised in both groups | n=223<br><br>People undergoing vascular surgery (aortic or aortoiliac and aneurysmectomy; aorto- femoral bypass for atherosclerotic disease; and femoropopliteal or femorodistal bypass)<br><br>Adults (mean age intervention 65±11 years, comparison 64±11 years)<br><br>Male to female ratio 200:43 | All-cause mortality (timepoint not reported)<br><br>DVT (10 days): confirmed by Duplex US, confirmed by venography<br><br>PE (timepoint not reported): confirmed by clinical suspicion investigated by angiogram<br><br>Thrombocytopaenia (timepoint not reported) | Numbers in each group for baseline data do not tally with text |
| Spebar 1981[275] | Intervention (n =24):<br>UFH (no further details reported)<br><br>Comparison (n=19):<br>No VTE prophylaxis | n=43<br><br>People undergoing peripheral vascular surgical procedures (including aortic reconstruction n=9, carotid artery reconstruction n=19, lumbar sympathectomy n=3, leg revascularisation n=4, psuedoaneurysm repair n=3, repair of artiovenous fistula n=2) | DVT (timepoint not reported): indicated by iodine-125 fibrinogen scanning<br><br>PE (timepoint not reported): no definition reported<br><br>Major bleeding (timepoint not reported): no definition reported | Data extracted from systematic review (Collins 1988 [61]) |

| Study | Intervention and comparison | Population | Outcomes | Comments |
|---|---|---|---|---|
| | | No further details reported | | |
| **Strata: limb amputation** | | | | |
| Lastoria 2006[190] | Intervention (n=41): LMWH (enoxaparin), 40mg 1x daily (standard dose). Timing: 12 hours before surgery or in emergency cases in the first postoperative day, until discharge.<br><br>Comparison (n=34): UFH, 5000IU administered subcutaneously. Timing: 12 hours before surgery or in emergency cases in the first postoperative day, until discharge. | n=75<br><br>People undergoing elective or emergency lower-limb amputation (n=30 above-knee; n=45 below-knee)<br><br>Adults (age range 18 to 86)<br><br>Male to female ratio 59:16 | DVT (5-8 days after surgery): confirmed by duplex scanning<br><br>Major bleeding (timepoint not reported): any 'bleeding complications' | Strata: lower limb amputation |
| **Strata: varicose veins** | | | | |
| Ayo 2017 [13] | Intervention (n = 39): AES (thigh high (30-40mmHg) for 24 hours post procedure and then daily during waking hours for 7 days)<br><br>Comparison (n = 46): Usual care, 24 hours of post-procedural bandages (no compression therapy) | n=85<br><br>People undergoing endovenous radiofrequency or laser ablation of great saphenous vein for valvular incompetence<br><br>USA<br><br>Mean age (SD not reported): compression: 52; usual care 49 years<br><br>Male to female ratio 20:65 | QOL: Venous clinical severity score (VCSS) at 7 days<br><br>QOL: Chronic venous insufficiency questionnaire (CIVIQ-2) at 90 days | Strata: varicose vein surgery<br><br>Some people were included in the study twice if they required bilateral treatment (number of people = 70, number of cases = 85) |
| San Norberto Garcia 2013[265] | Intervention (n=132): LMWH (Bemiparin, not UK licensed), 2500/3500IU 1x daily. Started 6 hours after wound closure, continued for 10 days +IPCD for first 7 days + AES (thigh length) + early mobilisation | n=264<br><br>People undergoing elective varicose vein surgery with moderate VTE risk (defined as having 2 risk factors for VTE)<br><br>Adults (mean 67; | DVT (90 days): confirmed by duplex ultrasound<br><br>PE (90 days): confirmed by duplex ultrasound<br><br>Major bleeding (90 days): fatal bleeding, | Strata: varicose vein surgery<br><br>Included people with moderate VTE risk (defined as having 2 risk factors for VTE); excluded people with high risk of |

| Study | Intervention and comparison | Population | Outcomes | Comments |
|---|---|---|---|---|
| | Comparison (n=130)<br>IPCD for first 7 days then AES (thigh length)<br>+ early mobilisation | range 18-75)<br><br>Male to female ratio 104:162<br><br>Spain | was into a critical organ (e.g. retropeitoneal, intracranial, intraocular, intraspinal), required reoperation, or was clinically over extrasurgical-site bleeding associated with a fall in haemoglobin of ≥20g/L, calculated from preoperated baseline value, or requiring infusion of ≥2U of whole blood or packed cells | bleeding |
| Wang 2015[306] | Intervention 1 (n=531):<br>UFH, 125U/kg, administered subcutaneously for 3 days<br><br>Intervention 2(n=550):<br>LMWH (Enoxaparin), 4000 IU, 1x daily (high dose) for 3 days<br><br>Comparison (n=542)<br>No VTE prophylaxis | n=1623<br><br>People undergoing varicose vein surgery (high ligation and stripping of the GSV, and removal of superficial varicosities)<br><br>Adults (mean age 47.62±10.37; range 23-68 years)<br><br>Male to female ratio: intervention 1 - 1:1.01;<br>2 – 1: 1.04;<br>3 – 1.09 : 1<br><br>China | DVT, proximal (30 days): confirmed by ultrasound<br><br>PE (30 days): computed tomography pulmonary angiography scan<br><br>Major bleeding (30 days): haemorrhage followed by discontinuation of anticoagulation therapy | Strata: varicose vein surgery |
| Ye 2016 [325] | Intervention (n = 200):<br>AES. Elastic bandage placed after the procedure and left in position during the first night. Patients then wore a thigh-high AES (class II, ankle pressure of 23-32 mmHg), during the daytime for at least 2 weeks.<br><br>Comparison (n = 200):<br>Elastic bandage placed | n=400<br><br>People undergoing endovenous ablation for primary unilateral great saphenous vein incompetence<br><br>China<br><br>Age, median (IQR):<br>Compression group 48 (37-59); usual care | All-cause mortality (14 days)<br><br>DVT (14 days): confirmed by ultrasound duplex<br><br>PE (14 days): definition not reported<br><br>QOL: Aberdeen Varicose Vein | Strata: varicose vein surgery |

| Study | Intervention and comparison | Population | Outcomes | Comments |
|---|---|---|---|---|
| | after the procedure and left in position during the first night (as in the intervention group). Then AES were not recommended | 49 (40-60)<br><br>Male to female ratio 165:235 | Symptom Severity Score (AVVSS) (28 days) | |

### 39.3.1 Strata: overall (not specified)

**Table 226: Clinical evidence summary: UFH compared to no prophylaxis**

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with No prophylaxis | Risk difference with UFH (95% CI) |
| DVT | 92 (2 studies) not reported | VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision | RR 0.57 (0.22 to 1.46) | 227 per 1000 | 98 fewer per 1000 (from 177 fewer to 105 more) |
| PE | 43 (1 study) not reported | VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision | Not estimable[d] | Not estimable[d] | 0 fewer per 1000 (from 0 fewer to 0 more)[d] |
| Major bleeding | 92 (2 studies) not reported | VERY LOW[a,c] due to risk of bias, indirectness, imprecision | RR 8.33 (1.13 to 61.7) | 23 per 1000 | 167 more per 1000 (from 3 more to 1000 more) |

a Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
c Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
d Zero events in both arms. Risk difference calculated in Review Manager

**Table 227: Clinical evidence summary: LMWH (standard dose pre-op/high dose post-op) compared to UFH**

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with UFH | Risk difference with LMWH (95% CI) |
| All-cause mortality | 233 | | RR 4.55 | 0 per 1000 | - |

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with UFH | Risk difference with LMWH (95% CI) |
| | (1 study)<br>not reported | VERY LOW[a,b,c]<br>due to risk of bias, indirectness, imprecision | (0.22 to 93.81) | | |
| DVT | 233<br>(1 study)<br>10 days | VERY LOW[a,b,c]<br>due to risk of bias, indirectness, imprecision | RR 2.27<br>(0.73 to 7.05) | 36 per 1000 | 46 more per 1000<br>(from 10 fewer to 218 more) |
| PE | 233<br>(1 study)<br>not reported | VERY LOW[a,b,c]<br>due to risk of bias, indirectness, imprecision | Not estimable[d] | Not estimable[d] | 0 fewer per 1000<br>(from 20 fewer to 20 more)[d] |
| Thrombocytopaenia | 233<br>(1 study)<br>not reported | VERY LOW[a,b,c]<br>due to risk of bias, indirectness, imprecision | Peto OR 6.81<br>(0.42 to 109.84) | 0 per 1000 | - |

a Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
c Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
d Zero events in both arms. Risk difference calculated in Review Manager

### 39.3.2 Strata: Varicose veins

**Table 228: Clinical evidence summary: LMWH +AES + IPCD + mobilisation versus IPCD/AES + mobilisation**

| Outcomes | No of | Quality of the evidence | Relative | Anticipated absolute effects |
|---|---|---|---|---|

| | Participants (studies) Follow up | (GRADE) | effect (95% CI) | Risk with IPCD/AES + mobilisation | Risk difference with LMWH +AES + IPCD mobilisation (95% CI) |
|---|---|---|---|---|---|
| DVT | 262 (1 study) 90 days | VERY LOW[b,c] due to risk of bias, imprecision | Not estimable[a] | Not estimable[a] | 0 fewer per 1000 (from 10 fewer to 10 more)[a] |
| PE | 262 (1 study) 90 days | VERY LOW[b,c] due to risk of bias, imprecision | Not estimable[a] | Not estimable[a] | 0 fewer per 1000 (from 10 fewer to 10 more)[a] |
| Major bleeding | 262 (1 study) 90 days | VERY LOW[b,c] due to risk of bias, imprecision | Not estimable[a] | Not estimable[a] | 0 fewer per 1000 (from 10 fewer to 10 more)[a] |

a Zero events in both arms. Risk difference calculated in Review Manager
b Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
c Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

**Table 229: Clinical evidence summary: LMWH (high dose) versus no prophylaxis**

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with No prophylaxis | Risk difference with LMWH (high dose) (95% CI) |
| DVT | 1092 (1 study) 30 days | HIGH | RR 0.07 (0.02 to 0.29) | 52 per 1000 | 48 fewer per 1000 (from 37 fewer to 51 fewer) |
| PE | 1092 (1 study) 30 days | HIGH | Peto OR 0.13 (0.03 to 0.53) | 15 per 1000 | 13 fewer per 1000 (from 7 fewer to 14 fewer) |
| Major bleeding | 1092 | | Peto OR 0.99 | 2 per 1000 | 0 fewer per 1000 |

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with No prophylaxis | Risk difference with LMWH (high dose) (95% CI) |
| | (1 study)<br>30 days | VERY LOW[a,b]<br>due to indirectness, imprecision | (0.06 to 15.78) | | (from 2 fewer to 26 more) |

a Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
b Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

**Table 230: Clinical evidence summary: UFH versus no prophylaxis**

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with No prophylaxis | Risk difference with UFH (95% CI) |
| DVT | 1073<br>(1 study)<br>30 days | HIGH | RR 0.11<br>(0.03 to 0.36) | 52 per 1000 | 46 fewer per 1000<br>(from 33 fewer to 50 fewer) |
| PE | 1073<br>(1 study)<br>30 days | HIGH | Peto OR 0.14<br>(0.03 to 0.55) | 15 per 1000 | 13 fewer per 1000<br>(from 7 fewer to 14 fewer) |
| Major bleeding | 1073<br>(1 study)<br>30 days | VERY LOW[a,b]<br>due to indirectness, imprecision | Peto OR 0.14<br>(0 to 6.96) | 2 per 1000 | 2 fewer per 1000<br>(from 2 fewer to 11 more) |

a Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes
b Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

**Table 231: Clinical evidence summary: LMWH (high dose) versus UFH**

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with UFH | Risk difference with LMWH (high dose) (95% CI) |
| DVT | 1081<br>(1 study)<br>30 days | LOW[a]<br>due to imprecision | RR 0.64<br>(0.11 to 3.84) | 6 per 1000 | 2 fewer per 1000<br>(from 5 fewer to 16 more) |
| PE | 1081<br>(1 study)<br>30 days | LOW[a]<br>due to imprecision | Not estimable[b] | Not estimable[b] | 0 fewer per 1000<br>(from 0 fewer to 0 more)[b] |
| Major bleeding | 1081<br>(1 study)<br>30 days | VERY LOW[a,c]<br>due to indirectness, imprecision | Peto OR 0.29<br>(0.05 to 1.68) | 8 per 1000 | 5 fewer per 1000<br>(from 7 fewer to 5 more) |

a Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
b Zero events in both arms. Risk difference calculated in Review Manager
c Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes

**Table 232: Clinical evidence summary: AES versus usual care**

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with Usual care | Risk difference with Varicose vein strata - AES (95% CI) |
| All-cause mortality | 400<br>(1 study)<br>2 weeks | VERY LOW[a,b]<br>due to risk of bias, imprecision | Not estimable | Moderate | |
| | | | | 0 per 1000 | 0 fewer per 1000<br>(from 10 fewer to 10 more)[a] |
| DVT<br>ultrasound duplex | 400<br>(1 study)<br>2 weeks | VERY LOW[a,b]<br>due to risk of bias, imprecision | Not estimable | Moderate | |
| | | | | 0 per 1000 | 0 fewer per 1000<br>(from 10 fewer to 10 more)[a] |
| Symptomatic pulmonary | 400 | | Not estimable | Moderate | |

| Outcomes | No of Participants (studies) Follow up | Quality of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with Usual care | Risk difference with Varicose vein strata - AES (95% CI) |
| embolism | (1 study)<br>2 weeks | VERY LOW[a,b]<br>due to risk of bias, imprecision | | 0 per 1000 | 0 fewer per 1000<br>(from 10 fewer to 10 more)[a] |
| HRQOL (AVVSS)<br>Aberdeen Varicose Vein Symptoms Severity Score. Scale from: 0 to 100.<br>Better=lower | 400<br>(1 study)<br>4 weeks | MODERATE[b]<br>due to risk of bias | | The mean HRQOL (AVVSS) in the control groups was 8 | The mean HRQOL (AVVSS) in the intervention groups was<br>0.5 higher<br>(0.19 lower to 1.19 higher) |
| HRQOL (VCSS)<br>Venous clinical severity score. Scale from: 0 to 30.<br>Better=lower | 85<br>(1 study)<br>7 days | VERY LOW[b,c,d]<br>due to risk of bias, indirectness, imprecision | | The mean HRQOL (VCSS) in the control groups was 4.35 | The mean HRQOL (VCSS) in the intervention groups was<br>1.23 lower<br>(4.72 lower to 2.26 higher) |
| HRQOL (CIVIQ-2)<br>Chronic venous insufficiency questionnaire. Scale from: 0 to 100.<br>Better=lower | 85<br>(1 study)<br>90 days | VERY LOW[b,c,d]<br>due to risk of bias, indirectness, imprecision | | The mean HRQOL (CIVIQ-2) in the control groups was 22.5 | The mean HRQOL (CIVIQ-2) in the intervention groups was<br>6.6 higher<br>(7.67 lower to 20.87 higher) |

a Zero events in both arms. Risk difference calculated in Review Manager
b Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
c Some people were included in the study twice if they required bilateral treatment (number of people = 70, number of cases = 85)
d Unable to calculate as standard deviations not reported

### 39.3.3 Strata: Lower limb amputation

**Table 233: Clinical evidence summary: LMWH (standard dose) versus UFH**

| Outcomes | No of Participants | Quality of the evidence | Relative | Anticipated absolute effects |
|---|---|---|---|---|

| | (studies)<br>Follow up | (GRADE) | effect<br>(95% CI) | Risk with<br>UFH | Risk difference with LMWH (standard dose)<br>(95% CI) |
|---|---|---|---|---|---|
| DVT | 75<br>(1 study)<br>5-8 days post-op | VERY LOW[a,b]<br>due to risk of bias, imprecision | RR 0.83<br>(0.22 to 3.07) | 118 per 1000 | 20 fewer per 1000<br>(from 92 fewer to 244 more) |
| Major bleeding | 75<br>(1 study)<br>not reported | VERY LOW[a,b,d]<br>due to risk of bias, indirectness, imprecision | Not estimable[c] | Not estimable[c] | 0 fewer per 1000<br>(from 50 fewer to 50 more)[c] |

a Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c Zero events in both arms. Risk difference calculated in Review Manager
d Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes

## 39.4 Economic evidence

**Published literature**

No relevant health economic studies were identified.

See also the health economic study selection flow chart in appendix F.

## 39.5 Evidence statements

**Clinical**

*Strata: overall (no specific vascular population defined)*

Very low quality evidence from two studies (n=92) suggested a possible clinical benefit with unfractionated heparin (UFH) compared to no prophylaxis for a reduction in DVT in people undergoing vascular surgery, however this finding is seriously imprecise and could also be consistent with an increase in DVT rates. A possible clinical harm with UFH was suggested with an increase in major bleeding, although this too was an imprecise estimate that could also have been consistent with no difference. No difference was noted between UFH and no prophylaxis for PE. Very low quality evidence from one study (n=233) suggested that there were worse outcomes for all-cause mortality, DVT and thrombocytopaenia when using LMWH at a standard dose pre-operatively followed by a high-dose post-operatively compared to using UFH. However there was considerable uncertainty around these results with all of them also being consistent with possible benefit.

*Strata: People undergoing surgery for varicose veins*

High quality evidence from one study (n=1092) showed a clinically important reduction in DVT and PE when using either high-dose LMWH or unfractionated heparin (UFH) compared to no prophylaxis. Very low quality evidence from the same study suggested no difference between the LMWH and no prophylaxis for major bleeding rates, and a possible benefit of UFH over no prophylaxis, although these findings were imprecise. When comparing high-dose LMWH to no prophylaxis, there was low quality evidence for a possible reduction in DVT and very low quality evidence for a possible reduction in major bleeding when using LMWH. However there was uncertainty around these results. No difference was found between the two for PE rates.

Very low quality evidence from one study (n=262) showed no difference in DVT, PE or major bleeding rates when comparing either stockings or intermittent pneumatic compression and early mobilisation with the same mechanical and mobilisation strategy plus the addition of LMWH.

Very low quality evidence from one study (n=400) found no difference in rates of DVT, PE and major bleeding when using anti-embolism stockings compared to no prophylaxis. Moderate quality evidence from the same study suggested no difference with respect of patient reported outcomes on the Aberdeen Varicose Vein Symptoms Severity Score. Very low quality evidence also suggested no difference in patient-reported scores on the Venous Clinical Severity Score and the Chronic Venous Insufficiency Questionnaire, although these findings were imprecise.

*Strata: Lower limb amputation*

Very low quality evidence from one study (n=75) suggested there was no difference between LMWH (standard dose) and UFH for the outcomes of DVT and major bleeding in those undergoing lower limb amputation. These findings were imprecise.

**Economic**

No relevant economic evaluations were identified.

## 39.6 Recommendations and link to evidence

### 39.6.1 Open vascular surgery or endovascular aneurysm repair

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| **Recommendations** | **1.5.49 Consider pharmacological VTE prophylaxis with LMWH[kk] for a minimum of 7 days for people who are undergoing open vascular surgery or major endovascular procedures, including endovascular aneurysm repair whose risk of VTE outweighs their risk of bleeding. [2018]**<br><br>**1.5.50 Consider mechanical VTE prophylaxis on admission for people who are undergoing open vascular surgery or major endovascular procedures, including endovascular aneurysm repair, if pharmacological prophylaxis is contraindicated. Choose either:**<br>• **anti-embolism stockings or**<br>• **intermittent pneumatic compression.**<br>**Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. [2018]** |
| **Research recommendation** | **None** |
| Relative values of different outcomes | The committee considered all-cause mortality (up to 90 days from hospital discharge), deep vein thrombosis (symptomatic and asymptomatic) (up to 90 days from hospital discharge), pulmonary embolism (symptomatic and asymptomatic) (up to 90 days from hospital discharge), fatal PE (up to 90 days from hospital discharge), and major bleeding (up to 45 days from hospital discharge) as critical outcomes.<br>The committee considered clinically relevant non-major bleeding (up to 45 days from hospital discharge), health-related quality of life (up to 90 days from hospital discharge), heparin-induced thrombocytopaenia (duration of study), and technical complications of mechanical interventions (duration of study) as important outcomes.<br>Please see section 4.4.3 in the methods chapter for further detail on prioritisation of the critical outcomes. |
| Quality of the clinical evidence | Three studies were included in this section, which were of different populations including people undergoing vascular surgery including aortic or aortoiliac aneurysm repair, aorto-femoral bypass for atherosclerotic disease, and femoropopliteal or femorodistal bypass; people undergoing elective aortic bifurcation graft surgery; and people undergoing aortic reconstruction, carotid artery surgery, lumbar sympathectomy, leg revascularisation, psuedoaneurysm repair and repair of artiovenous fistulae.<br>All of the evidence was of very low quality for both UFH compared to no prophylaxis, and for LMWH compared to UFH. This was due to risk of bias, indirectness and imprecision. The outcomes for both studies were downgraded for indirectness as the |

[kk] At the time of publication (March 2018), LMWH did not have a UK marketing authorisation for use in young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

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| | definition of the outcome of the study or the timepoint at which the outcome was measured did not match the protocol or was not reported. For DVT, both studies specified this was confirmed by fibrinogen scanning, which the committee did not consider to be an accurate measure of confirmation. |
| Trade-off between clinical benefits and harms | Many people having major arterial surgery are older and potentially immobile, putting them at risk for VTE. However many will already be receiving anticoagulation or antiplatelet therapy and therefore be at greater risk of bleeding or admitted with bleeding as emergencies. In addition, full dose heparin is frequently administered during surgery for arterial disease prior to arterial clamping. Major aortic procedures are done either by open techniques or more minimally invasive endovascular techniques but both tend to be long procedures often lasting several hours and both are associated with a significant risk of VTE. Post-operatively return to full mobility can be significantly delayed after vascular surgery especially for open procedures. The committee noted that there was little RCT evidence in the open vascular surgery population but given their likelihood of extended immobility they considered it would be appropriate for clinicians to consider pharmacological prophylaxis with LMWH for those at low risk of bleeding. For those people whose risk of bleeding outweighs their risk of VTE, the committee agreed mechanical prophylaxis could be considered. Given the lack of evidence identified for different forms of mechanical prophylaxis the committee considered it would best to offer clinicians the choice between AES and IPC. Most people who are vascular patients will have peripheral arterial disease; this means they are not usually able to use AES. Intermittent compression can be used but may impair postoperative mobilisation and rehabilitation.<br>Mechanical prophylaxis is recommended until the patient is back to normal mobility as the committee consider that mechanical prophylaxis offers little benefit once a patient is mobile. Pharmacological prophylaxis is recommended for a minimum of 7 days because the average duration of trials extrapolated from the abdominal surgery was between 7 and 10 days. |
| Trade-off between net clinical effects and costs | No economic studies were identified for this review. The unit costs were presented to the committee. The committee considered the clinical evidence presented for each stratum alongside the unit costs presented.<br><br>Based on the doses reported in the included clinical studies, the cost of using UFH (Heparin sodium) ranged from £9 to £59. Using the BNF recommended dose the cost was £24.6 (assuming administration for 7 days). For LMWH (enoxaparin sodium) the cost ranged from £24 to £91 (based on the included studies' doses). Using the BNF recommended dose the cost was £24.2 (assuming administration for 7 days). The cost of nurse time required for administration was higher for UFH compared to LMWH due to the higher frequency of administration. UFH also required more monitoring tests (full blood count).<br>Hence, LMWH was recommended as the preferred pharmacological prophylaxis modality as it was considered to be more cost effective, given the reduced frequency of administration and need for monitoring.<br>For those with contraindications to pharmacological prophylaxis, it was noted that AES are unlikely to be suitable due to the likelihood having peripheral arterial disease. In the absence of other suitable mechanical options the committee considered that IPC would be the only potential option and is likely to be cost effective in this population given their high VTE risk. |
| Other considerations | None. |

### 39.6.2 Lower limb amputation

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| **Recommendations** | **1.5.51 Consider pharmacological VTE prophylaxis with LMWH[ll] for a minimum of 7 days for people who are undergoing lower limb amputation whose risk of VTE outweighs their risk of bleeding. [2018]**<br><br>**1.5.52 Consider mechanical VTE prophylaxis with intermittent pneumatic compression on the contralateral leg, on admission, for people who are undergoing lower limb amputation and if pharmacological prophylaxis is contraindicated. [2018]**<br><br>**1.5.53 For people undergoing lower limb amputation, continue mechanical VTE prophylaxis until the person no longer has significantly reduced mobility relative to their anticipated mobility. [2018]** |
| **Research recommendation** | **None** |
| Relative values of different outcomes | The committee considered all-cause mortality (up to 90 days from hospital discharge), deep vein thrombosis (symptomatic and asymptomatic) (up to 90 days from hospital discharge), pulmonary embolism (symptomatic and asymptomatic) (up to 90 days from hospital discharge), fatal PE (up to 90 days from hospital discharge), and major bleeding (up to 45 days from hospital discharge) as critical outcomes.<br>The committee considered clinically relevant non-major bleeding (up to 45 days from hospital discharge), health-related quality of life (up to 90 days from hospital discharge), heparin-induced thrombocytopaenia (duration of study), and technical complications of mechanical interventions (duration of study) as important outcomes.<br>Please see section 4.4.3 in the methods chapter for further detail on prioritisation of the critical outcomes. |
| Quality of the clinical evidence | One study comparing LMWH to UFH was included. The quality of the data for DVT as an outcome was very low due to risk of bias and imprecision, and very low for major bleeding as this was additionally downgraded for indirectness as this was defined as any 'bleeding complications'. |
| Trade-off between clinical benefits and harms | There was a lack of direct evidence for the amputation population but those undergoing lower limb amputation are known to have a very high risk of VTE in the amputated leg due to surgical trauma and ligation of the vein, and they will be relatively immobile both before and after the surgery which also puts them at higher risk of VTE in the non-amputated leg. Most people who are vascular patients having amputation will have peripheral arterial disease; this means they are not usually able to use AES on the contralateral limb and not at all on the side of the amputation. Likewise, intermittent pneumatic compression can only be used on the contralateral limb. In view of their high risk and the unsuitability of mechanical methods, extrapolation from evidence in other high risk groups means it is likely that these patients will need pharmacological prophylaxis. If there is the occasional person who has a high bleeding risk such that pharmacological prophylaxis cannot be used, then due to their high risk of VTE they should receive mechanical prophylaxis on the contralateral leg.<br>Mechanical prophylaxis is recommended until the patient is back to normal mobility |

[ll] At the time of publication (March 2018), LMWH did not have a UK marketing authorisation for use in young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

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| | as the committee consider that mechanical prophylaxis offers little benefit once a patient is mobile. Pharmacological prophylaxis is recommended for a minimum of 7 days because the average duration of trials extrapolated from the abdominal surgery was between 7 and 10 days. |
| Trade-off between net clinical effects and costs | No economic studies were identified for this review. The unit costs were presented to the committee. The committee considered the clinical evidence presented for each stratum alongside the unit costs presented.<br>The clinical evidence showed that there was no clinical difference for LMWH compared to UFH with regard to DVT and major bleeding. Given the lower cost of LMWH compared to UFH it was considered to be the cost effective option, being equally effective and less costly. |
| Other considerations | None. |

### 39.6.3 Varicose vein surgery

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| **Recommendations** | **1.5.54 Be aware that VTE prophylaxis is generally not needed for people undergoing varicose vein surgery where:**<br>• **total anaesthesia time is less than 90 minutes and**<br>• **the person is at low risk of VTE. [2018]**<br><br>**1.5.55 Consider pharmacological VTE prophylaxis with LMWH[mm], starting 6-12 hours after surgery and continuing for 7 days for people undergoing varicose vein surgery if:**<br>• **total anaesthesia time is more than 90 minutes or**<br>• **the person's risk of VTE outweighs their risk of bleeding. [2018]**<br><br>**1.5.56 Consider mechanical VTE prophylaxis with anti-embolism stockings, on admission, for people undergoing varicose vein surgery:**<br>• **who are at increased risk of VTE and**<br>• **when pharmacological prophylaxis is contraindicated. [2018]**<br><br>**1.5.57 If using anti-embolism stockings for people undergoing varicose vein surgery, continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. [2018]** |
| **Research recommendation** | **None** |
| Relative values of different outcomes | The committee considered all-cause mortality (up to 90 days from hospital discharge), deep vein thrombosis (symptomatic and asymptomatic) (up to 90 days from hospital discharge), pulmonary embolism (symptomatic and asymptomatic) (up to 90 days from hospital discharge), fatal PE (up to 90 days from hospital discharge), and major bleeding (up to 45 days from hospital discharge) as critical outcomes. |

[mm] At the time of publication (March 2018), LMWH did not have a UK marketing authorisation for use in young people under 18 for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

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| | The committee considered clinically relevant non-major bleeding (up to 45 days from hospital discharge), health-related quality of life (up to 90 days from hospital discharge), heparin-induced thrombocytopaenia (duration of study), and technical complications of mechanical interventions (duration of study) as important outcomes.<br>Please see section 4.4.3 in the methods chapter for further detail on prioritisation of the critical outcomes. |
| Quality of the clinical evidence | Four studies were included that looked at prophylaxis in people undergoing varicose vein surgery.<br>One study (San Noberto 2013) focused on comparing mechanical prophylaxis (IPCD then AES) with and without LMWH. All of the evidence was of very low quality due to risk of bias and imprecision.<br>Another study (Wang 2015) compared both LMWH, UFH and no prophylaxis. Some evidence was of high quality; however the majority of evidence was of very low quality. The evidence for both LMWH versus no prophylaxis, and for UFH versus no prophylaxis with regards to DVT and PE, was of high quality, however the evidence for major bleeding was of low quality due to indirectness of the outcome definition. The evidence for LMWH compared to UFH with regards to DVT, PE and major bleeding was all of low quality due to imprecision. The committee noted that Wang 2015 used open vein surgery for varicose veins, which is not a type of surgery recommended by NICE for this condition.<br>Two further studies (Ayo 2017 and Ye 2016) compared anti-embolism stockings with no compression which were assessed as high risk of bias due to selection concerns and high rates of missing data. Some of the evidence was also downgraded due to intervention indirectness as patients were included in the study twice if they required bilateral treatment. Evidence was further downgraded due to imprecision around the effect estimates for the quality of life outcomes. |
| Trade-off between clinical benefits and harms | Varicose vein surgery is a relatively common procedure as varicose veins affect a large proportion of the population. The majority of people undergoing surgery for varicose veins are women; therefore oral contraceptive use and hormone replacement therapy use are common in this surgical population. Open varicose vein surgery is now becoming less common and more surgery is being performed using minimally invasive catheter techniques, often under local anaesthetic. People undergoing varicose vein surgery are considered to be at risk for VTE, and DVT and PE are the most common serious complications related to varicose vein surgery. The committee considered that the risk is high enough that pharmacological prophylaxis should be considered for at risk persons undergoing varicose vein surgery. Anti-embolism stockings were considered to be the preferred mechanical prophylaxis strategy in this population as they are usually mobile and not suitable for IPC.<br>Mechanical prophylaxis is recommended until the patient is back to normal mobility as the committee believe that mechanical prophylaxis offers little benefit once a patient is mobile. Pharmacological prophylaxis is recommended for a minimum of 7 days because the average duration of trials extrapolated from the abdominal surgery was between 7 and 10 days. |
| Trade-off between net clinical effects and costs | No economic studies were identified for this review. The unit costs were presented to the committee. The committee considered the clinical evidence presented for each stratum alongside the unit costs presented.<br>The clinical evidence showed a possible benefit of LMWH for DVT and major bleeding but no difference for PE when compared with UFH. Given the lower cost of LMWH, it was considered to be the dominant pharmacological prophylaxis option in this population (more effective and less costly). |
| Other considerations | The committee noted that the rate of symptomatic DVT in varicose vein surgery is low, and that trials with a large number of participants are needed to reflect the true |

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| | rate of DVT. This committee noted that the low number of participants in the included studies meant that the studies did not accurately represent the rate of DVT in this population. |