34 Major trauma

34.1 Introduction

The majority of patients suffering major trauma require assessment and management by the orthopaedic trauma service. There may be associated injury to the head, chest or abdomen in those patients sustaining poly-trauma, most frequently occurring following road traffic collisions. However, major pelvic and spinal injuries and multiple long bone fractures in isolation constitute significant orthopaedic trauma. A proportion will require management in a critical care setting, in either an intensive care or high dependency unit, for which additional guidance can be found in Chapter 20 of this guideline.

For major trauma patients, the main concern is the constantly changing balance between the initial risk of bleeding and the subsequent increased risk of thrombotic events. Trauma patients have been identified to be at increased risk of VTE.

More guidance related to VTE prophylaxis for patients with single injury musculoskeletal trauma can be found in the chapters on lower limb immobilisation (chapter 24), fragility fractures of the pelvis, hip and proximal femur (chapter 25), foot and ankle surgery (chapter 29) and spinal injury (chapter 33) in this guideline.

34.2 Review question: What is the effectiveness of different pharmacological and mechanical prophylaxis strategies (alone or in combination) for people with major trauma?

For full details see review protocol in appendix C.

Table 150: PICO characteristics of review question

Population	Adults and young people (16 years and older) who are attending hospital with major trauma

Interventions	Mechanical:
	• Anti-embolism stockings (AES) (above or below knee)
	• Intermittent pneumatic compression (IPCD) devices (full leg or below knee)
	• Foot pumps or foot impulse devices (FID)
	• Electrical stimulation (including Geko devices)
	• Continuous passive motion
	• Vena caval filters
	
	Pharmacological:
	• Unfractionated heparin (UFH) (low dose, administered subcutaneously)
	• Low molecular weight heparin (LMWH), licensed in UK:
	  ○ enoxaparin (standard prophylactic dose 40 mg daily; minimum 20 mg daily* to maximum 60 mg twice daily*)
	  ○ 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*)
	  ○ tinzaparin (standard prophylactic dose 3500-4500 units once daily; minimum 2500 units once daily* to maximum 4500 units twice daily*; obese patients – maximum 6750 twice daily*)
	• LMWH, licensed in countries other than UK:

	○ Bemiparin (standard 2500 units daily; minimum 2500 units daily to maximum 3500 units daily) ○ Certoparin (3000 units daily) ○ Nadroparin (standard 2850 units once daily; minimum 2850 units once daily to maximum up to 57 units/kg once daily) ○ Parnaparin (standard 3200 units once daily; minimum 3200 units once daily to maximum 4250 units once daily) ○ Reviparin (minimum 1750 units once daily to maximum 4200 units once daily) • Vitamin K Antagonists: ○ warfarin (variable dose only) ○ acenocoumarol (all doses) ○ phenindione (all doses) • Fondaparinux (all doses)* • Apixaban (all doses)* • Dabigatran (all doses)* • Rivaroxaban (all doses)* • Aspirin (up to 300 mg)* *off-label
Comparisons	Compared to: • Other VTE prophylaxis treatment, including monotherapy and combination treatments (between class comparisons for pharmacological treatments only) • No VTE prophylaxis treatment (no treatment, usual care, placebo) Within intervention (including same drug) comparisons, including: • Above versus below knee stockings • Full leg versus below knee IPC devices • Standard versus extended duration prophylaxis. • Low versus high dose for LMWH • Preoperative versus post-operative initiation of LMWH
Outcomes	Critical outcomes: • All-cause mortality (up to 90 days from hospital discharge) • 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) • Pulmonary embolism (symptomatic and asymptomatic) (up to 90 days from hospital discharge) (NMA outcome). 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 • 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 • 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 Important outcomes: • 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. • Health-related quality of life (validated scores only)(up to 90 days from hospital discharge) • Heparin-induced thrombocytopaenia (HIT) (duration of study) • Technical complications of mechanical interventions (duration of study)
Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs.

34.3 Clinical evidence

A search was conducted for randomised trials comparing the effectiveness of mechanical and pharmacological prophylaxis strategies (alone or in combination) in people with major trauma. Of the five studies included in the previous guideline conducted in the major trauma population (CG92), four studies were included[112,113,166,278], and one study was excluded.[60] Six new studies were also included.[9,74,82,103,165,173] Additionally the committee decided that vena caval filters would only be appropriate for consideration for VTE prophylaxis in the major trauma population, therefore the studies included in the previous guideline on the effectiveness of vena caval filters were considered here. There was one study[73] noted for consideration in CG92, however this was excluded in this guideline as it looked at the effectiveness of vena caval filters for secondary prevention of VTE. The included studies are summarised in Table 151 below. See also the study selection flow chart in appendix E, forest plots in appendix L, study evidence tables in appendix H, GRADE tables in appendix K and excluded studies list in appendix N.

Table 151: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Anglen 1998[9]	Intervention (n=68): IPCD, below knee Comparison (n=49): foot pump, applied to both feet (intermittent plantar compression devices, Plexipulse foot pumps) Applied after surgery or in the case of significant preoperative delay, before surgery	n=117 People with trauma (pelvis 10.3%, hip 6.8% , acetabulum 32.5%, femur 43.6%, combination 6.8% fracture, multi trauma 61.5%) ISS not reported Age >17 years Males and females (65:52) United States	DVT (up to 14 days): confirmed by duplex ultrasound PE (2 months): method of confirmation not reported	Major trauma status not defined as no ISS data reported.
Dennis 1993[74]	Intervention 1 (n=189): IPCD, full leg Device applied within 48 hours of injury, until discharge or fully ambulatory Intervention 2 (n=92):	n=395 People with trauma (chest 29.9%, abdomen 23.3%, extremities 47.6%, head 23.3%, spinal cord 12.7%, paralysis	All-cause mortality (time-point not reported) DVT (time-point not reported): confirmed by duplex scanning or Doppler ultrasound	Trauma inclusion defined as ISS >9 Patients had scanning at 48 hrs and then

Study	Intervention and comparison	Population	Outcomes	Comments
	UFH (5000U 2 x daily) Started within 96 hours of injury, until discharge or fully ambulatory <u>Comparison (n=114):</u> no VTE prophylaxis	6.3%) ISS >9 Age >18 years Gender not reported United States	PE (time-point not reported): confirmed by duplex scanning or Doppler ultrasound Fatal PE (time-point not reported): confirmed by autopsy	every 5 days after injury for between 2-25 scans
Elliot 1999[82]	<u>Intervention (n=74):</u> IPCD, full leg Duration not reported <u>Comparison (n=75):</u> foot pump (plantar venous intermittent pneumatic compression devices) Duration not reported	n = 149 People with major trauma (head 82.6%, face 24.8%, chest 55.7%, abdomen 26.2%, upper limb 13.4%, other 38.9%) ISS: intervention mean, SD = 31, 11.6; comparison mean, SD = 30.2, 13.1 Age >13 years Males and females (100:49) United States	All-cause mortality (time-point not reported) DVT (8 days): confirmed by compression duplex ultrasonography Major bleeding (time-point not reported): definition not reported	
Fuchs 2005[103]	<u>Intervention (n=111):</u> • Continual passive motion, 2 x daily • UFH 5000U 3 x daily <u>Comparison (n=116):</u> UFH 5000U 3 x daily Treatment started on the evening before surgery or immediately following surgery in emergency cases, carried on until mobilisation	n = 227 People with bony or ligamentous trauma to the spine, pelvis, femur, tibia or ankle ISS not reported Age >18 years Males and females (131:96) Germany	All-cause mortality (3 months) DVT (3 months): confirmed by compression ultrasonography, Doppler and/or plethysmography, and venography PE (3 months): method of confirmation not reported	Major trauma status not defined as no ISS data reported.
Geerts 1996[112]	<u>Intervention (n=136):</u> UFH 5000U, given subcutaneously every 12 hours Duration: within 36 hours of the injury for up to 14 days.	n=265 People with major trauma (head 4.9%, face/chest/abdomen 37.7%, spine 15%, lower limb 54.3%)*	All-cause mortality (14 days) DVT (days 10-14):confirmed by venography	Trauma inclusion defined as ISS >9

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=129): LMWH, high dose (enoxaparin), 30 mg, given subcutaneously every 12 hours Duration: within 36 hours of the injury for up to 14 days.	ISS >9 Age (mean, SD): intervention group 37.0 (16.5), comparison group 39.1 (16.8) Males and females (192:73) Canada *some patients had injuries at more than one site	PE, symptomatic (14 days): confirmed by ventilation perfusion scan Major bleeding (14 days): defined as overt bleeding that was associated with a decrease in the haemoglobin level of at least 2g per decilitre, the transfusion of two or more units of packed red cells, an intracranial or retroperitoneal site of bleeding, or the need for surgical intervention Fatal PE (14 days): confirmed by autopsy	
Ginzburg 2003[113]	Intervention (n=224): IPCD, below knee Duration: within 24hrs of trauma until walking independently or discharge from hospital. Maximum 8 consecutive hours disuse allowed Comparison (n=218): LMWH, high dose (enoxaparin), 30 mg, given subcutaneously every 12 hours Duration: within 24 hours of the injury until walking independently or discharge from hospital	n=442 People with high risk trauma (head 22.9%, spinal cord 7.5%, chest 37.3%, leg or pelvis fracture 35.1%)* ISS >9 Age (mean): intervention group 40, comparison group 42) Males and females (327:115) United states *some patients had injuries at more than one site	All-cause mortality (30 days) DVT (30 days): confirmed by Doppler ultrasonography PE, symptomatic (30 days): confirmed by spiral computed tomography or ventilation-perfusion scintigraphy Major bleeding (30 days): defined as haemorrhage leading to a fall in haemoglobin conc. of 2 g/dl, transfusion of 2 or more of packed red blood cells, intracranial or retroperitoneal bleeding or bleeding requiring surgical intervention	Includes moderately (ISS 9-19) and severely (ISS >19) injured people.

Study	Intervention and comparison	Population	Outcomes	Comments
Knudson 1994[165]	Group 1 (patients who could receive either methods of prophylaxis): Intervention 1 (n=44): UFH (5000U, 2 x daily) Intervention 2 (n=32): • IPCD, full leg • AES, undefined Comparison (n=64): No VTE prophylaxis Duration not reported	n=251 People with trauma (laparotomy, thoracotomy, ventilated > 24 hours, spine, pelvic, femur fracture) Mean ISS 16 (range 10-66) Age > 18 years Males and females (200:51) United States	All-cause mortality DVT (3 weeks): confirmed by duplex imaging PE (3 weeks): confirmed by pulmonary angiography	Cause of major trauma unclear for all patients Unclear if patients in group 3 received AES
	Group 2 (patients who could not wear mechanical prophylaxis devices): Intervention (n=19): UFH (5000U, 2 x daily) Comparison (n=27): No VTE prophylaxis Duration not reported			
	Group 3 (patients who had contraindication to heparin): Intervention (n=26): IPCD, full leg Comparison (n=39): No VTE prophylaxis Duration not reported			
Knudson 1996[166]	Intervention (n=120): LMWH, high dose (enoxaparin) 30mg given subcutaneously every 12 hours Duration not reported Comparison (n=82): • IPCD, length undefined • AES, length undefined Or FID alone	n=202 People with trauma injuries (venous injury, pelvic fracture, unstable spine, spinal fracture) ISS > 10 Age (mean): 38.5 years Male and female (values not reported)	All-cause mortality (time-point not reported) DVT (time-point not reported): confirmed by venous duplex ultrasound PE (time-point not reported): method of confirmation not reported Fatal PE (time-point not reported): confirmed by	Trauma inclusion defined as ISS >10 Different mechanical prophylaxis used depending on the condition of the lower extremity.

Study	Intervention and comparison	Population	Outcomes	Comments
	Sequential gradient pneumatic compression sleeves worn over AES, or arteriovenous impulse device Duration not reported	United States	autopsy	
Kurtoglu 2004[173]	Intervention (n = 60): • LMWH, standard dose (enoxaparin) 40mg given once daily • IPCD, below knee Comparison (n = 60): IPCD, below knee All patients received IPCD on admission, and initiation of LMWH was determined after CT within 24 hours of admission. Duration not reported	n = 120 People with severe head/spinal trauma (head 90.1%, spinal 9.1%) ISS 4-35 Age >14 years Male and female: 47:73 Turkey	All-cause mortality (time-point not reported) DVT (time-point not reported): confirmed by duplex sonography PE (time-point not reported): confirmed by spiral CT Major bleeding (time-point not reported): defined as macroscopic haematuria without renal injury, overt bleeding, and a sudden drop in haemoglobin level (>2 g/dl) Fatal PE (time-point not reported): confirmed by spiral CT	No definition of 'severe' trauma provided.
Stannard 2006[278]	Intervention (n=97): LMWH, high dose (enoxaparin), 30mg, given subcutaneously every 12 hours Duration: within 24-48 hours of the injury Comparison (n=103): Pulsatile foot pumps at time of admission (patients asked to use it for at least 12 hours per day) combined with enoxaparin (high dose, 30mg every 12 hours) on a delayed basis (5 days after admission)	n=200 People with recent blunt skeletal trauma (mean ISS 14.42, range 4-57) Age >18 years United States	All-cause mortality (time point not reported) DVT (24 hours before discharge): confirmed by bilateral magnetic resonance venography and ultrasonography PE, symptomatic (time point and method of confirmation not reported) Fatal PE (time point and method of confirmation not reported)	Blunt trauma

Table 152: Clinical evidence summary: IPCD (full leg) versus no prophylaxis

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD (full leg) versus no prophylaxis (95% CI)
All-cause mortality	368 (2 studies) 7-90 days	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.3 (0.06 to 1.62)	26 per 1000	18 fewer per 1000 (from 25 fewer to 16 more)
DVT (symptomatic and asymptomatic)	368 (2 studies) 7-90 days	LOW[a] due to risk of bias	RR 0.26 (0.1 to 0.7)	98 per 1000	73 fewer per 1000 (from 29 fewer to 88 fewer)
PE	368 (2 studies) 7-90 days	VERY LOW[b] due to risk of bias, imprecision	Peto OR 0.07 (0 to 4.01)	7 per 1000	6 fewer per 1000 (from 7 fewer to 19 more)
Fatal PE	303 (1 study) 7-90 days	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 0.59 (0.03 to 10.34)	9 per 1000	4 fewer per 1000 (from 9 fewer to 75 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 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 153: Clinical evidence summary: IPCD (full leg) versus foot pump

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD (full leg) versus foot pump (95% CI)
All-cause mortality	149 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 1.22 (0.39 to 3.81)	67 per 1000	15 more per 1000 (from 41 fewer to 187 more)
DVT (symptomatic and asymptomatic)	124 (1 study)	VERY LOW[a,b,c] due to risk of bias,	RR 0.31 (0.11 to 0.89)	210 per 1000	145 fewer per 1000 (from 23 fewer to 187 fewer)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD (full leg) versus foot pump (95% CI)
	8 days	indirectness, imprecision			
Major bleeding	149 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	Peto OR 7.49 (0.15 to 377.48)	0 per 1000	Not estimable[d]

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 Downgraded by 1 increment if the outcome definition reported did not meet definition of outcome in protocol
d Could not be calculated as there were no events in the comparison group

Table 154: Clinical evidence summary: IPCD (below knee) versus foot pump

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD (below knee) versus foot pump (95% CI)
DVT (symptomatic and asymptomatic)	117 (1 study) up to 14 days	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 0.17 (0.02 to 1.76)	44 per 1000	36 fewer per 1000 (from 43 fewer to 31 more)
PE	117 (1 study) 2 months	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 0.18 (0 to 9.51)	15 per 1000	12 fewer per 1000 (from 15 fewer to 110 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 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 155: Clinical evidence summary: IPCD (full leg) + AES (undefined) versus no prophylaxis

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD full leg + AES versus no prophylaxis (95% CI)
All-cause mortality	96 (1 study) up to 3 weeks	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[c]	Not estimable[c]	0 fewer per 1000 (from 47 fewer to 47 more)[d]
DVT (symptomatic and asymptomatic)	96 (1 study) up to 3 weeks	VERY LOW[a,b] due to risk of bias, imprecision	RR 4 (0.77 to 20.69)	31 per 1000	94 more per 1000 (from 7 fewer to 615 more)
PE	96 (1 study) up to 3 weeks	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 0.22 (0 to 14.26)	16 per 1000	12 fewer per 1000 (from 16 fewer to 169 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 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c Could not be calculated as there were no events in the intervention or comparison group
d Risk difference calculated in Review Manager

Table 156: Clinical evidence summary: Continual passive motion + UFH versus UFH

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Continual passive motion + UFH versus UFH (95% CI)
All-cause mortality	227 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[c]	Not estimable[c]	0 fewer per 1000 (from 17 fewer to 17 more)[d]
DVT (symptomatic and asymptomatic)	227 (1 study) 3 months	MODERATE[a] due to risk of bias	RR 0.14 (0.05 to 0.4)	250 per 1000	215 fewer per 1000 (from 150 fewer to 237 fewer)
PE	227	VERY LOW[a,b]	Not	Not	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 Control	Risk difference with Continual passive motion + UFH versus UFH (95% CI)
	(1 study) 3 months	due to risk of bias, imprecision	estimable[c]	estimable[c]	(from 17 fewer to 17 more)[d]

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 Could not be calculated as there were no events in the intervention or comparison group
d Risk difference calculated in Review Manager

Table 157: 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 Control	Risk difference with UFH versus no prophylaxis (95% CI)
All-cause mortality	360 (3 studies) up to 3 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.32 (0.06 to 1.64)	24 per 1000	17 fewer per 1000 (from 23 fewer to 16 more)
DVT (symptomatic and asymptomatic)	360 (3 studies) up to 3 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.47 (0.17 to 1.26)	68 per 1000	36 fewer per 1000 (from 57 fewer to 18 more)
PE	360 (3 studies) up to 3 month	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 0.17 (0.01 to 2.88)	10 per 1000	8 fewer per 1000 (from 10 fewer to 18 more)
Fatal PE	206 (1 study) 7-90 days	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 1.24 (0.08 to 20.32)	9 per 1000	2 more per 1000 (from 8 fewer to 144 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 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 158: Clinical evidence summary: UFH versus IPCD (full leg)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD (full leg) versus UFH (95% CI)
All-cause mortality	281 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 1.03 (0.09 to 11.18)	11 per 1000	0 fewer per 1000 (from 10 fewer to 108 more)
DVT (symptomatic and asymptomatic)	281 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 1.23 (0.3 to 5.05)	33 per 1000	6 more per 1000 (from 19 fewer to 107 more)
PE	281 (1 study) time-point 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 17 fewer to 17 more)[e]
Fatal PE	281 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	Peto OR 2.20 (0.11 to 42.32)	11 per 1000	6 more per 1000 (from 5 fewer to 178 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 increment if the outcome definition reported did not meet definition of outcome in protocol

c Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

d Could not be calculated as there were no events in the intervention or comparison group

e Risk difference calculated in Review Manager

Table 159: Clinical evidence summary: UFH versus IPCD (full leg) + AES (undefined)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD full leg + AES versus UFH (95% CI)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with IPCD full leg + AES versus UFH (95% CI)
All-cause mortality	76 (1 study) up to 3 weeks	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[c]	Not estimable[c]	0 fewer per 1000 (from 52 fewer to 52 more)[d]
DVT (symptomatic and asymptomatic)	76 (1 study) up to 3 weeks	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.18 (0.02 to 1.55)	125 per 1000	102 fewer per 1000 (from 123 fewer to 69 more)
PE	76 (1 study) up to 3 weeks	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[c]	Not estimable[c]	0 fewer per 1000 (from 52 fewer to 52 more)[d]

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 Could not be calculated as there were no events in the intervention or comparison group

d Risk difference calculated in Review Manager

Table 160: Clinical evidence summary: LMWH (standard dose; standard duration) + IPCD (below knee) versus IPCD (below knee)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH (standard dose) + IPCD versus IPCD (95% CI)
All-cause mortality	120 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 1.14 (0.44 to 2.95)	117 per 1000	16 more per 1000 (from 65 fewer to 228 more)
DVT (symptomatic and asymptomatic)	120 (1 study) time-point not	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 0.75 (0.18 to 3.21)	67 per 1000	17 fewer per 1000 (from 55 fewer to 147 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH (standard dose) + IPCD versus IPCD (95% CI)
	reported				
PE	120 (1 study) time point 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 32 fewer to 32 more)[e]
Major bleeding	120 (1 study) time point 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 32 fewer to 32 more)[e]
Fatal PE	120 (1 study) time point not reported	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision	RR 2 (0.38 to 10.51)	33 per 1000	33 more per 1000 (from 21 fewer to 317 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 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c Downgraded by 1 increment if the outcome does not fit the protocol
d Could not be calculated as there were no events in the intervention or comparison group
e Risk difference calculated in Review Manager

Table 161: Clinical evidence summary: LMWH (high dose; standard duration) versus UFH

Outcomes	No of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus UFH (95% CI)
All-cause mortality	344 (1 study) 14 days	LOW[a] due to imprecision	Peto OR 7.52 (0.47 to 120.72)	0 per 1000	Not estimable[b]
DVT (symptomatic and asymptomatic)	265 (1 study)	MODERATE[a] due to imprecision	RR 0.7 (0.51 to 0.97)	441 per 1000	132 fewer per 1000 (from 13 fewer to 216 fewer)

Outcomes	No of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus UFH (95% CI)
	10-14 days				
PE	265 (1 study) 14 days	LOW[a] due to imprecision	Peto OR 7.8 (0.15 to 393.69)	0 per 1000	Not estimable[b]
Major bleeding	344 (1 study) 14 days	MODERATE[a] due to imprecision	Peto OR 3.92 (0.78 to 19.63)	6 per 1000	17 more per 1000 (from 1 fewer to 97 more)
Fatal PE	344 (1 study) 14 days	LOW[a] Due to imprecision	Not estimable[c]	Not estimable[c]	0 more per 1000 (from 113 fewer to 113 more)[d]

a Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
b Could not be calculated as there were no events in the comparison group
c Could not be calculated as there were no events in the intervention or comparison group
d Risk difference calculated in Review Manager

Table 162: Clinical evidence summary: LMWH (high dose; standard duration) versus IPCD (below knee)

Outcomes	No of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus IPCD (95% CI)
All-cause mortality	442 (1 study) 30 days	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[c]	Not estimable[c]	0 more per 1000 (from 88 fewer to 88 more)[d]
DVT (symptomatic and asymptomatic)	442 (1 study) 30 days	LOW[a,b] due to risk of bias, imprecision	Peto OR 0.24 (0.05 to 1.07)	27 per 1000	20 fewer per 1000 (from 25 fewer to 2 more)
PE	442 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 1.03 (0.06 to 16.48)	4 per 1000	0 more per 1000 (from 4 fewer to 64 more)

Outcomes	No of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus IPCD (95% CI)
	30 days				
Major bleeding	442 (1 study) 30 days	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.03 (0.26 to 4.06)	18 per 1000	1 more per 1000 (from 13 fewer to 55 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 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c Could not be calculated as there were no events in the intervention or comparison group
d Risk difference calculated in Review Manager

Table 163: Clinical evidence summary: LMWH (high dose; standard duration) versus (IPCD, undefined + AES, undefined) or FID

Outcomes	No of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus (IPCD + AES) or FID (95% CI)
All-cause mortality	202 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, imprecision, indirectness	Not estimable[c]	Not estimable[c]	0 per 1000 (from 202 fewer to 202 more)[d]
DVT (symptomatic and asymptomatic)	202 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, imprecision, indirectness	Peto OR 0.34 (0.03 to 3.40)	24 per 1000	16 fewer per 1000 (from 24 fewer to 54 more)
PE	202 (1 study) time-point not reported	VERY LOW[a,b,c] due to risk of bias, imprecision, indirectness	Not estimable[c]	Not estimable[c]	0 per 1000 (from 202 fewer to 202 more)[d]

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

Outcomes	No of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus (IPCD + AES) or FID (95% CI)

c Downgraded by 1 increment if the outcome definition reported did not meet definition of outcome in protocol
d Could not be calculated as there were no events in the intervention or comparison group
e Risk difference calculated in Review Manager

Table 164: Clinical evidence summary: LMWH (high dose; standard duration) versus delayed LMWH (high dose; standard duration) + foot pump

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus LMWH + foot pump (95% CI)
All-cause mortality	200 (1 study) time-point not reported	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[d]	Not estimable[d]	0 per 1000 (from 194 fewer to 194 more)[e]
DVT (symptomatic and asymptomatic)	200 (1 study) time-point not reported	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.53 (0.69 to 3.43)	87 per 1000	46 more per 1000 (from 27 fewer to 212 more)
PE	200 (1 study) time-point not reported	VERY LOW[a,b] due to risk of bias, imprecision	Peto OR 7.94 (0.49 to 128.04)	0 per 1000	Not estimable[c]
Fatal PE	200 (1 study) time-point not reported	VERY LOW[a,b] due to risk of bias, imprecision	Not estimable[d]	Not estimable[d]	0 per 1000 (from 194 fewer to 194 more)[e]

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

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with LMWH versus LMWH + foot pump (95% CI)
c Could not be calculated as there were no events in the comparison group d Could not be calculated as there were no events in the intervention or comparison group e Risk difference calculated in Review Manager					

34.4 Economic evidence

Published literature

Two health economic studies were identified with the relevant comparison, and have been included in this review.[51,198] One of these two studies was previously included in CG92. [198] The two studies are summarised in the health economic evidence profiles below (Table 165 and Table 166) and the health economic evidence tables in appendix J.

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

Table 165: Health economic evidence profile: VCF vs IPCD

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Carter Chiasson 2009[51] [(Canada)]	Partially applicable [(a)]	Potentially serious limitations [(b)]	**-Study design:** cost-utility analysis using decision analytic modelling. **-Population:** Adult (>/= 15 years)Trauma patients with severe injuries admitted to the ICU who were believed to have a contraindication to pharmacological VTE prophylaxis for up to 2 weeks because of a risk of major bleeding. **-Interventions** 1. Pneumatic compression devices (IPCD) and expectant management alone during the first 2 weeks. 2. IPCD as well as weekly Serial Doppler ultrasound (SDU) screening for the duration of hospitalisation beginning in the first week of ICU admission. **(results not reported here)** **3.** Prophylactic insertion of vena-cava filter (VCF).	3 vs 1 £975	3 vs 1 0.0 QALYs	IPCD less costly	A wide range of one-way sensitivity analyses was undertaken. None of the SAs changed the conclusion

Abbreviations: ICER: incremental cost-effectiveness ratio; ICU: intensive care unit; IPCD: pneumatic compression device; QALY: quality-adjusted life years; RCT: randomised controlled trial; SAs: sensitivity analyses; VCF: vena-cava filter; VTE: venous thromboembolism.

(a) Uncertainty regarding the applicability of unit costs from Canada, in 2007 to current NHS context. The discount used is 5% for both costs and outcomes; however, this was tested in a sensitivity analysis with a range of 0-6%. It is not clear which utility measure was used to derive the utility values used in the model.

(b) The health states included in the long term of the model does not seem to include CTEPH as a complication of PE. Baseline risks as well as relative effectiveness are based on the results of an observational cohort and single RCT so by definition, not reflective of all the evidence in this area. Both local and national unit costs were used in the analysis, so may not be generalisable. Utility values were not tested in sensitivity analysis.

Table 166: Health economic evidence profile: LMWH (low dose) vs UFH (low dose)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Lynd 2007[198] ([Canada])	Partially applicable [(a)]	Potentially serious limitations [(b)]	**- Study design:** cost-consequences analysis using decision analytic modelling. **- Population:** Patients with major trauma (trauma score of =>9) **- Interventions:** 1. UFH 5000 units once daily. 2. LMWH (enoxaparin 30 mg once daily).	2 vs 1 £47	2 vs 1 **LYG:** 130 life-years lost per 1000 **DVT:** 86 DVTs averted per 1000 **PE**: 18 PEs averted per 1000 patients **MB**: 18 more MB events per 1000 patients **Deaths:** 7 fewer deaths per 1000 patients	2 vs 1 **LYG:** Dominated (more costly and less effective) **DVT**: £553 per DVT averted **PE:** £2,611 per PE averted **MB:** Dominated (more costly and less effective) **Deaths**: £6,714 per death averted	Probabilistic and deterministic (one-way and two-way) sensitivity analyses were conducted. The model results were robust to all changes.

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial; UFH: unfractionated heparin.

a) Uncertainty regarding the applicability of unit costs from Canada, in 2003 to current NHS context. The discount used is 5% for outcomes; however, this was tested in a sensitivity analysis with a range of 3-7%. QALYs were not used as outcome.

b) The health states included in the long term of the model do not include CTEPH and PTS. Baseline risks as well as relative effectiveness are based on the results of a single RCT (Geerts 1996[112]) so by definition, not reflective of all the evidence in this area. Both local and national unit costs were used in the analysis, so may not be generalisable.

34.5 Evidence statements

Clinical

Mechanical prophylaxis

When IPCD (full leg) was compared to no prophylaxis, evidence from two studies (n=368) showed there was a clinical benefit of IPCD for DVT. And suggested benefit for all other outcomes including all-cause mortality, PE and fatal PE. However the non-DVT outcomes were all associated with imprecision. The quality of the evidence ranged from very low to low due to risk of bias and imprecision.

The study comparing IPCD (full leg) in combination with AES with no prophylaxis (n=96) found a possible clinical harm of IPCD + AES for DVT, and a possible clinical benefit for PE. However there was imprecision associated with these results. There was no clinical difference for all-cause mortality. The quality of the evidence was very low due to risk of bias and imprecision.

For the comparison of IPCD (full leg) versus foot pump, evidence from one study (n=149) suggested clinical benefit of IPCD for DVT, but a possible clinical harm for major bleeding, however there was imprecision around these results. There was no clinical difference in terms of all-cause mortality. For below knee IPCD compared to foot pump, the evidence from another single study (n=117) demonstrated a possible clinical benefit for IPCD for both DVT and PE, but there was imprecision around the results. The quality of the evidence for both comparisons ranged from very low to low due to risk of bias and imprecision.

Mechanical versus pharmacological prophylaxis

When IPCD (full leg) was compared to UFH (single study, n=281), there was a suggested clinical benefit of IPCD for fatal PE, and no clinical difference for all other reported outcomes including all-cause mortality, DVT and PE. However there was uncertainty surrounding these results. The quality of the evidence was very low due to risk of bias, imprecision and indirectness.

For the comparison of IPCD (full leg) in combination with AES versus UFH (single study, n=76), there was a possible clinical harm of IPCD in combination with AES for DVT, and no clinical difference for all-cause mortality or PE. However this evidence was very low quality due largely to the very serious imprecision surrounding the effect estimates.

For the comparison of continual passive motion in combination with UFH versus UFH alone (single study, n=227), there was clinical benefit of continual passive motion for DVT, and no clinical difference for all-cause mortality and PE. The quality of the evidence ranged from very low to moderate due to risk of bias and imprecision.

When LMWH (standard dose) in combination with IPCD (below-knee) was compared to IPCD (below-knee), evidence from one study (n=120) suggested a clinical benefit of LMWH for DVT, and a suggested clinical harm for fatal PE. There was no clinical difference for all-cause mortality, PE and major bleeding. However for all results there was uncertainty around the effect estimates. The quality of the evidence was very low due to risk of bias, imprecision and indirectness.

When LMWH (high dose) was compared to IPCD (below-knee), evidence from one study (n=442) suggested clinical benefit of LMWH for DVT, however no clinical difference for all-cause mortality, PE and major bleeding. There was considerable uncertainty around all these results. The quality of the evidence ranged from very low to low due to risk of bias and imprecision.

The study comparing LMWH (high dose) to (IPCD in combination with AES) or FID (n=202) found a suggested clinical benefit of LMWH for DVT, and no clinical difference for all-cause mortality and PE.

There was considerable uncertainty around all these results. The quality of the evidence was very low due to risk of bias, imprecision and indirectness.

For the comparison of LWMH (high dose) versus delayed LMWH (high dose) in combination with foot pump, the evidence from one study (n=200) suggested a possible clinical harm for LMWH for both DVT and PE, and no clinical difference for all-cause mortality and fatal PE, however all these results had considerable uncertainty.

Pharmacological prophylaxis

For the comparison of UFH versus no prophylaxis, evidence from 3 studies (n=360) suggested clinical benefit of UFH for all-cause mortality, DVT and PE. However these results were very seriously imprecise and associated with both no difference and harm as well. No clinical difference was found for fatal PE. The quality of the evidence was very low due to risk of bias and imprecision.

For the comparison of LWMH (high dose) versus UFH, the evidence from one study (n=344) suggested a possible clinical harm of LMWH for all-cause mortality, PE and major bleeding, however the evidence was very imprecise and also consistent with no difference and possible benefit. However there was a possible clinical benefit of LMWH for DVT, although this was also consistent with no difference. There was no clinical difference in terms of fatal PE. The quality of the evidence ranged from low to moderate due to imprecision.

Economic

One cost–utility analysis found that in trauma patients with severe injuries admitted to the ICU, pneumatic compression devices and expectant management alone was less costly and equally effective, compared to prophylactic insertion of vena-cava filter for VTE prophylaxis. This analysis was assessed as partially applicable with potentially serious limitations.

One cost-consequences analysis found that in patients with major trauma low molecular weight heparin (low dose) was more costly (£47 more per patient) and had 0.086 fewer DVT events per patient, 0.0018 fewer PE events per patient and 0.007 fewer deaths per patient but 0.0018 more major bleeding events per patient and 0.013 fewer life-years gained per patient compared to unfractionated heparin (low dose) for VTE prophylaxis. This analysis was assessed as partially applicable with potentially serious limitations.

34.6 Recommendations and link to evidence

Recommendations	**1.5.34 Offer mechanical VTE prophylaxis with intermittent pneumatic compression on admission to people with serious or major trauma. Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. [2018]** **1.5.35 Reassess risk of VTE and bleeding in people with serious or major trauma whenever their clinical condition changes and at least daily. [2018]** **1.5.36 Consider pharmacological VTE prophylaxis for people with serious or major trauma as soon as possible after the risk assessment when the risk of VTE outweighs the risk of bleeding. Continue for a minimum of 7 days. [2018]**
Research	**None**

recommendation	
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. 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. Please see section 4.4.3 in the methods chapter for further detail on prioritisation of the critical outcomes.
Quality of the clinical evidence	Ten studies were included in this review. Four were included in the previous guideline (CG92) and six were new studies. A total of thirteen comparisons were identified from the ten included studies, evaluating mechanical (IPCD, AES, continual passive motion and foot pump) and pharmacological (UFH and LMWH) interventions for VTE prophylaxis. The committee discussed that the generalisability of evidence from studies to individual patients should be considered. The trials included moderate to severe trauma patients with a wide range of ISS levels reported (if at all) and a variety of injuries, with the more severe patients usually managed in specialised trauma centres. There is a range of risks for VTE and bleeding, depending on the type, location and severity of the injuries. The majority of the evidence was downgraded due to risk of bias based on inadequate randomisation and allocation concealment. Much of the evidence was further downgraded due to imprecision. In cases where major bleeding was not adequately defined, the evidence from these studies was also downgraded for indirectness of the outcome.
Trade-off between clinical benefits and harms	The committee noted that the high event rate for DVT and PE in this population compared to some of the other review populations is expected. This tallies with clinical experience; it is common for ICU populations to experience higher rates of DVT and PE. Therefore clinicians are likely to be comfortable with the idea of administering VTE prophylaxis in this population. The committee noted that the trauma population are likely to have significant immobilisation due to the nature of their injuries which would contribute to an increased risk for VTE. Evidence was identified for both mechanical and pharmacological prophylaxis both compared to each other and to no VTE prophylaxis. When considering the evidence for mechanical prophylaxis, the committee noted that the evidence showed some possible clinical benefits of IPCD alone or in combination with AES for the outcomes of all-cause mortality, DVT and PE, however there was uncertainty around these results consistent with no difference, or harm. There were seven comparisons of mechanical versus pharmacological prophylaxis. This evidence demonstrated conflicting findings, with some suggesting clinical benefits of mechanical prophylaxis or combined mechanical and pharmacological prophylaxis for DVT, PE and fatal PE, and other evidence demonstrating clinical benefits of pharmacological prophylaxis for DVT. The committee discussed that for the major trauma population, the risk of bleeding is high, and therefore mechanical prophylaxis may be preferable. It was also noted that AES are not always practical in the major trauma population, due to the nature of the injuries which may prevent AES from being worn (for example injuries involving broken legs). The committee discussed different prophylaxis strategies including immediate combined mechanical and pharmacological prophylaxis or initial mechanical and then switching to pharmacological once bleeding risk had minimised. While the review sought to find any differences between the effectiveness of IPCD

	and foot-pumps, in practice foot-pumps are understood to be a subset (type) of intermittent pneumatic compression device, specifically shaped for the foot only. The committee considered that the evidence did not clearly demonstrate clinical superiority of half- or full-leg based IPCD compared to foot pumps and therefore decided it was reasonable to group all such devices under the more general term of intermittent pneumatic compression. The committee concluded that mechanical prophylaxis such as IPCD and foot pumps should be recommended as initial treatment, until the risk of bleeding is reduced, at which time the risk of bleeding should be weighed against the risk of VTE. Given the lack of evidence for AES alone and the practical issues surrounding its use, the committee concluded that AES would not be recommended. There were two pharmacological prophylaxis only comparisons. When UFH was compared to no prophylaxis, possible clinical benefits of UFH were seen for all-cause mortality, DVT and PE. However, when UFH was compared to LMWH, the evidence was mixed and therefore the committee considered that there was insufficient evidence to specify which type of pharmacological prophylaxis was most effective for this population. It was highlighted that if necessary (for example reoperation) anticoagulation with UFH can be reversed, unlike with LMWH or fondaparinux. The committee concluded that pharmacological prophylaxis should be considered for major trauma patients, but did not specify which type of pharmacological prophylaxis should be used. The particular prophylaxis preparation used would need to be based on clinical judgement on consideration of the individual patient factors. The committee also discussed whether pharmacological prophylaxis should be given in addition to or as an alternative to mechanical prophylaxis, however it was agreed that this would need to depend on a clinical judgement taking into account the individual patient.
Trade-off between net clinical effects and costs	Two economic studies have been included in this review. One study comparing LMWH to UFH was previously included in CG92. The second study compared VCFs to IPCDs in trauma patients who have contraindications to pharmacological prophylaxis. Both studies were assessed as partially applicable with potentially serious limitations. The committee discussed the economic evidence alongside the clinical evidence. It was acknowledged that the serious and major trauma populations are at very high risk of bleeding, hence mechanical prophylaxis options will have a more favourable benefit-harm balance, particularly in the early stages of the trauma event. The economic evidence presented supported the cost effectiveness of IPCD and showed that it was a cost saving option compared to VCFs in people who have contraindication to pharmacological prophylaxis. The committee considered that, based on the evidence presented and their collective clinical experience, the use of VCFs for primary prevention of VTE in this population is not a cost-effective use of resources. They also acknowledged that the removal of VCF incurs extra cost that has not been included in the economic evidence presented and this is likely to make VCFs even more costly. Hence, the committee chose to recommend against their use for the purpose of primary VTE prevention in this population. For people at low risk of major bleeding, the committee considered that the benefit of pharmacological prophylaxis in the prevention of VTE is likely to outweigh their risks. Therefore, the committee considered the addition of pharmacological prophylaxis in this group to be a cost-effective use of resources and likely to be off-set through the prevention of costly VTE events.
Other considerations	It was noted that the studies included in this review include populations with varying degrees of injury severity. Initially the committee considered including only those papers with patients with major trauma defined as Injury Severity Score ≥16.[15] However in keeping in line with the NICE Major Trauma guideline (https://www.nice.org.uk/guidance/ng39) this definition was extended to include major trauma by definition of included study. The committee discussed that in the UK context having an ISS of ≥9 gets patient details entered onto TARN (trauma

	audit and research network). Once the ISS is getting into the high teens this represents multi-system injuries. The committee highlighted that reassessment of VTE and bleeding risk needed to happen on an at least daily basis in this population due to the nature of their injuries and evolving risk profile. The committee also considered the use of vena caval filters, however due to the lack of clinical evidence and the presence of economic evidence demonstrating it not to be cost effective it was decided not to recommend this method of prophylaxis. For people undergoing neurosurgery as a result of a head injury see the recommendations relating to cranial surgery insection 32.6.