38 Thoracic surgery

38.1 Introduction

Thoracic surgery involves the repair of organs located in the thorax, or chest. Factors that may alter the risk of VTE in people undergoing thoracic surgery:

- After lung resection, pulmonary embolism to the remaining lung carries a commensurately higher risk of death.
- Most patients who have video-assisted thorascopic surgery (VATS), particularly for pneumothorax, are young (less than 30 years) and are able to walk around the ward up to the time of surgery and soon after and have short lengths of stay.

There are no special factors that increase the risk of bleeding or the hazard associated with it in thoracic surgery. There are no other special factors that would affect the choice of, and use of, specific methods of VTE prophylaxis in thoracic surgery.

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

For full details see review protocol in appendix C.

Table 222: PICO characteristics of review question

Population	Adults and young people (16 years and older) undergoing thoracic surgery who are admitted to hospital, and outpatients post-discharge
Intervention(s)	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 Pharmacological (no minimum duration): • Unfractionated heparin (UFH) (low dose, administered subcutaneously) • Low molecular weight heparin (LMWH), licensed in UK: ○ enoxaparin (standard prophylactic dose 40mg daily; minimum 20mg daily* to maximum 60mg 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 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), acenocoumarol (all doses), phenindione (all doses) • Fondaparinux (all doses) • Apixaban (all doses) • Dabigatran (all doses) • Rivaroxaban (all doses) • Aspirin (up to 300mg)* *off-licence
Comparison(s)	• 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)
Outcomes	Critical outcomes: • All-cause mortality (up to 90 days from hospital discharge) (NMA outcome) • Deep vein thrombosis (symptomatic and asymptomatic) (7-90 days from hospital discharge). Confirmed by: radioiodine fibrinogen uptake test; venography; Duplex (Doppler) ultrasound; MRI; Impedance Plethysmography (used as rule out tool) (NMA outcome) • Pulmonary embolism (7- 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 (NMA outcome) • 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 (NMA outcome) • 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

38.3 Clinical evidence

No relevant clinical studies comparing different pharmacological and mechanical prophylaxis strategies for people undergoing thoracic surgery were identified. Papers included in the previous guideline (CG92) in the major surgery review were considered for inclusion in addition to papers identified in the update.

38.4 Economic evidence

Published literature

One health economic study was identified with the relevant comparison and has been included in this review.[305] This is summarised in the health economic evidence profile below (Table 223) and the health economic evidence tables in appendix J.

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

Table 223: Health economic evidence profile: LMWH (standard dose, standard duration) + AES (knee-length) vs LMWH (standard dose , standard duration) + AEs (thigh-length) vs LMWH (standard dose, standard duration)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost-effectiveness	Uncertainty
Wade 2015[305] ([UK])	Partially applicable [(a)]	Potentially serious limitations [(b)]	- **Study type**: CUA using decision modelling - **Population**: Patients undergoing any general surgery (subgroups considered were high risk patients, medium risk patients and low risk patients). - **Interventions:** **Intervention 1:** LMWH (for duration of 7 days (standard duration). **Intervention 2:** Knee-length AES in addition to LMWH for a duration of 7 days (standard duration). **Intervention 3:** Thigh-length AES in addition to pharmacological prophylaxis (LMWH) for duration of 7 days (standard duration).	**High risk patients:** 1 (vs 3) : £176 2 (vs 3): £177 3: comparator	**High risk patients:** 1 (vs 3): 0.009 QALYs lost 2 (vs 3) : 0.007 QALYs lost 3: comparator	**High risk patients:** LMWH + thigh-length AES (intervention 3) dominant (less costly and more effective)	The results of all scenario and sensitivity analyses were largely consistent with the base case analysis for all subgroups

Abbreviations: AES: anti-embolism stockings; CUA: cost utility analysis; ICER: incremental cost-effectiveness ratio; LMWH: low molecular weight heparin; QALY: quality-adjusted life years; RCT: randomised controlled trial

(c) Mixed population of all surgery types, however subgroup analysis is also presented.

(d) The model did not include some relevant health outcomes; e.g. clinically-relevant non-major bleeding , minor bleeding and surgical site infection.

38.5 Evidence statements

Clinical

No relevant clinical studies were identified.

Economic

- One cost-utility analysis found that for VTE prophylaxis in high risk general surgery patients, LMWH (standard dose, standard duration) + thigh-length AES was dominant (less costly and more effective) compared to LMWH (standard dose, standard duration) alone and to LMWH (standard dose, standard duration)+ AES (knee-length). This analysis was assessed as partially applicable with potentially serious limitations.

38.6 Recommendations and link to evidence

Recommendations	**1.5.46 Consider VTE prophylaxis for people undergoing thoracic surgery who are at increased risk of VTE. [2018]** **1.5.47 Start mechanical VTE prophylaxis on admission for people undergoing thoracic surgery. Choose either:** • **anti-embolism stockings or** • **intermittent pneumatic compression.** **Continue until the person no longer has significantly reduced mobility relative to their normal or anticipated mobility. [2018]** **1.5.48 Consider adding pharmacological VTE prophylaxis for people undergoing thoracic surgery for a minimum of 7 days to people whose risk of VTE outweighs their risk of bleeding:** • **Use LMWH[hh] as first-line treatment.** • **If LMWH[ii] is contraindicated use fondaparinux sodium[jj]. [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) (7-90 days from hospital discharge), pulmonary embolism (7- 90 days from hospital discharge), major bleeding (up to 45 days from hospital discharge) and fatal PE (7- 90 days from

[hh] 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.

[ii] 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.

[jj] At the time of publication (March 2018), fondaparinux sodium did not have a UK marketing authorisation 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.

	hospital discharge) as critical outcomes. The committee considered health-related quality of life (up to 90 days from hospital discharge), clinically relevant non-major bleeding (up to 45 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	No clinical evidence was identified for this review.
Trade-off between clinical benefits and harms	In the previous guideline this group was considered together with other major abdominal surgery (gastrointestinal, bariatric, gynaecological, urological). For the update the committee wished to explore if there was any evidence specifically for the thoracic surgery population because it was considered to be different clinically to the abdominal surgery population both in terms of the procedures involved and the fact that the chest and not the abdomen or pelvis that was being operated on. In the absence of direct evidence the committee considered it would be reasonable to extrapolate the recommendations from the abdominal surgery population to this population, including the strength of the recommendation as this is a high risk group. However the use of fondaparinux sodium in the thoracic surgery population is off-label as fondaparinux sodium did not have a UK marketing authorisation for this indication at the time of consultation (October 2017). Therefore the committee recommend LMWH in the first instance and fondaparinux sodium only if LMWH is contraindicated. Following lung resection, the risk of PE in the remaining lung is higher. Some patients having certain types of thoracic surgery (for example video-assisted thorascopic surgery) are younger, are mobile up to the time of surgery and soon after. 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 to specifically cover thoracic surgery patients; however, one economic study that has been included in the major abdominal surgery review covered the general surgical population stratified according to the risk of VTE. The committee considered that this evidence can be applicable to the thoracic surgery population, specifically the “high risk” subgroup. The study is a cost-utility analysis for standard duration prophylaxis. It was assessed as partially applicable with potentially serious limitations. This analysis showed that combined prophylaxis using LMWH + AES (thigh length) was dominant (more effective and less costly) compared to single prophylaxis with LMWH only (standard dose, standard duration) only and combined prophylaxis of LMWH (standard dose, standard duration)+ AES (knee-length). The committee discussed whether the evidence was enough to recommended either knee or thigh length AES. The economic evidence supported the cost effectiveness of combined prophylaxis that includes thigh-length AES, however the committee noted that thigh-length AES are less convenient for people to wear and are more difficult to fit. Hence, the committee agreed that the choice of the length of stocking should be made taking into account the preference of the individual and his/her ability to adhere to wearing them. IPCD was also recommended as an alternative option that requires less nursing time in terms of fitting and monitoring. The committee also agreed that both LMWH and fondaparinux should be recommended as pharmacological options to address issues of contraindications and individual preferences. As fondaparinux use in this population is off-licence it should

	only be considered where LMWH is contraindicated.
Other considerations	The 'consider' recommendation is a reflection of the lack of evidence in this population. However, it is the committee's view that for this group of patients, prophylaxis is likely to be most clinically and cost effective for those assessed to be at high risk of VTE.