14 People with acute coronary syndromes

14.1 Introduction

Patients diagnosed with acute coronary syndromes (ACS) are treated with anti-thrombotics. These treatments primarily consist of aspirin, clopdidogrel or other thienopyridines and heparin. The duration of each therapy varies, with aspirin often being life-long, clopidogrel in the order of 12 months and heparin for a period of three to five days post-event. Dual antiplatelet agents are also often given for a period which may be for up to a year after drug eluting coronary stent insertion. If full dose anticoagulation is stopped the protection it provides diminishes, allowing an increased risk of VTE. The VTE effectiveness of dual antiplatelet regimes remains largely unstudied in this context but will increase bleeding risk.

14.2 Review question: What is the effectiveness of different pharmacological and mechanical prophylaxis strategies (alone or in combination) for people being treated for acute coronary syndromes (using anticoagulants and/or antiplatelet agents)?

For full details see review protocol in appendix C.

Table 72: PICO characteristics of review question

Population	Adults and young people (16 years and older) being treated for acute coronary syndromes with anticoagulants and/or antiplatelet agents who are: • Admitted to hospital • Having day procedures • Discharged from hospital • Outpatients post-discharge
Intervention(s)	Mechanical: • Anti-embolism stockings (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 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

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	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 300mg)* *off-label
Comparison(s)	Treatment for acute coronary syndromes (antiplatelet agents; anticoagulants; antiplatelet agents and anticoagulants) plus VTE prophylaxis treatment, versus treatment for acute coronary syndromes plus one of the following: • 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
Outcomes	Critical outcomes: • All-cause mortality (up to 90 days from hospital discharge) • Deep vein thrombosis (symptomatic and asymptomatic) (7-90 days from hospital discharge) (NMA outcome). Confirmed by: radioiodine fibrinogen uptake test; venography; Duplex (Doppler) ultrasound; MRI; Impedance Plethysmography (used as rule out tool) • 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 • 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

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	• Fatal PE (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 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 thrombocytopenia (HIT) (duration of study) ○ Technical complications of mechanical interventions (duration of study)
Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs.

14.3 Clinical evidence

No relevant clinical studies comparing the effectiveness of different pharmacological and mechanical prophylaxis strategies (alone or in combination) for people with acute coronary syndromes. See the study selection flow chart in appendix E and excluded studies list in appendix N. Seven studies that were included in CG92 were excluded from the review. Reasons for exclusion include incorrect population, incorrect intervention, incorrect study design and no relevant outcomes [20, 70, 92, 153], [15 55 195].

14.4 Economic evidence

Published literature

No relevant health economic studies were identified.

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

14.5 Evidence statements

Clinical

No relevant clinical studies were identified.

Economic

No relevant economic evaluations were identified.

14.6 Recommendations and link to evidence

Recommendations	**1.4.1 Be aware that people receiving anticoagulant drugs as part of their treatment for an acute coronary syndrome do not usually need VTE prophylaxis. See also recommendation 1.3.17. [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

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	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 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 thrombocytopenia (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 relevant clinical evidence identified. The committee noted that the studies that were previously included in the review were published in the 1970s/80s and that treatment for acute coronary syndromes has since changed. Based on this the committee agreed that these studies are no longer applicable and decided to exclude them.
Trade-off between clinical benefits and harms	No relevant clinical evidence was identified. The committee noted that people treated for acute coronary syndromes will be on anticoagulant agents to manage their condition. These agents would also act as prophylaxis against VTE. Consequently, the committee considered there is no need to offer additional pharmacological prophylaxis when these agents are being used (even though the level of anticoagulation with rivaroxaban/fondaparinux is not therapeutic). The committee also noted that some of these patients may be on dual or triple antiplatelet therapy and adding prophylaxis could increase the risk of bleeding. For this population of people with acute coronary syndromes, the committee decided to cross-refer to the recommendations for people using anticoagulation and people using antiplatelet agents. The committee also noted that there was no evidence examining the effectiveness of mechanical prophylaxis. Without any evidence the committee decided not to offer additional mechanical prophylaxis to patients taking vitamin K agonists or receiving full anticoagulation therapy.
Trade-off between net clinical effects and costs	No relevant economic studies were identified. Unit costs of pharmacological and mechanical prophylaxis were presented to the committee (see appendix Q). The committee acknowledged that this population will be receiving therapeutic doses of anticoagulation and additional prophylaxis is unlikely to offer a clinical benefit. The committee considered the possible side effects and the additional cost of prescribing prophylaxis to this population and considered that offering additional prophylaxis to this population is unlikely to be cost effective.
Other considerations	The committee note that further guidance on the peri-operative management of patients on anticoagulation and antiplatelet therapy, including advice on when to restart their treatment, is provide in the British Society for Haematology guidance on Peri-operative management of anticoagulation and antiplatelet therapy published in 2016 (available from http://onlinelibrary.wiley.com/doi/10.1111/bjh.14344/full) which provides more detail on interrupting anticoagulation treatments.

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