J.13 Acutely ill medical patients

Study	[National Clinical Guideline Centre 2010[666]]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design**: Decision analytic model **Approach to analysis:** A decision tree model was developed based on the results of a systematic literature review and a network meta-analysis. **Perspective:** UK NHS and PSS **Time horizon:** VTEs and major bleeding events modelled for the acute period 10 days). QALYs and health service costs arising from these events are modelled over the patient's lifetime **Treatment effect**	**Population:** Adult (18 years or older) admitted as general medical admissions to hospitals in England. **Cohort settings:** Start age: 74 years Male: 47% **Intervention 1:** No prophylaxis **Intervention 2:** LMWH (average of dalteparin 5000 units sc daily) and enoxaparin (4000 units subcutaneously daily) **Intervention 3:** UFH (5000 units three times daily) **Intervention 4:**	**Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2–1): NR (95% CI: NR; p=NR) **Currency & cost year:** 2009 UK pounds **Cost components incorporated:** Pharmacological prophylaxis costs, prophylaxis testing, nurse time, VTE diagnosis and treatment costs, other events treatment costs (i.e. stroke, PTS, CTEPH, major bleeding, reoperation)	**QALYs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2–1): NR (95% CI: NR; p=NR)	**Incremental net monetary benefit (INMB) (pa)** **Intervention 1:** £0 (comparator) **Intervention 2:** £328 **Intervention 3:** £118 **Intervention 4:** -£61 Probability cost-effective (£20K threshold): **Intervention 1:** 1.7% **Intervention 2:** 72.3% **Intervention 3:** 17.7% **Intervention 4:** 8.3% **Analysis of uncertainty:** Deterministic and probabilistic sensitivity analyses were performed. The deterministic SAs explored the impact of changing the incidence of CTEPH and PTS and their costs, including HIT, changing its incidence, lower costs for LMWH, changing fatality rate after PE and MB and change the cost effectiveness threshold.

duration:[a] 10 days **Discounting:** Costs: 3.5% ; Outcomes: 3.5%	Fondaparinux sodium (2.5 mg subcutaneously)			A two-way threshold analysis exploring the impact of baseline risk for both major bleeding and PE was also undertaken. In all SAs, the most cost effective strategy remained the same (LMWH), except where high bleeding baseline risk and low PE baseline risk were used, where no prophylaxis was the most cost effective strategy.

Data sources

Health outcomes: baseline events were obtained from the no prophylaxis arm of the RCTs included in the systematic review and NMA that informed the model. Relative treatment effects for DVT (symptomatic and asymptomatic), PE (symptomatic) and major bleeding. **Quality-of-life weights:** utilities based on the EQ-5D UK tariff were sourced from the published literature and previous guidelines. **Cost sources:** standard sources on unit costs in the UK were used including the drug tariff, the NHS reference costs and the BNF.

Comments

Source of funding: National Institute for Health and Care Excellence (NICE). **Limitations:** Some uncertainty regarding the applicability of unit costs from 2009 to current NHS context. The relative treatment effect applied to all VTE events in the model is the relative treatment effect obtained from the DVT NMA.

Overall applicability:[b] Directly applicable   **Overall quality**[c] Potentially serious limitations

Abbreviations: BNF: British National Formulary; 95% CI: 95% confidence interval; CTEPH: chronic thromboembolic pulmonary hypertension; CUA: cost-utility analysis; da: deterministic analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); HIT: Heparin induced thromboembolism; ICER: incremental cost-effectiveness ratio; LMWH: low molecular weight heparin; NR: not reported; NMA: network meta-analysis; pa: probabilistic analysis; PE: pulmonary embolism; QALYs: quality-adjusted life years; SA: sensitivity analysis; UFH: unfractionated heparin.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

Study	[Millar 2016[640]]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CCA (health outcomes: years of	**Population:** Adult patients admitted to	**Total cost**[b] **(mean per patient):**	**Deaths**[b] **(mean per patient):**	**ICER:** DVTs

life lost, non-fatal VTE events avoided)

Study design: decision tree model

Approach to analysis: a decision tree model was designed based on the results of the PREVENT trial.

Perspective: Australian public health care system

Follow-up: inpatient admission period

Treatment effect duration:[a] same as follow-up

Discounting: Costs: n/a ; Outcomes: 3%

Australian hospital as medical inpatients.

Cohort settings:
Start age: 74 years
Male: NR

Intervention 1:
No VTE prophylaxis.

Intervention 2:
VTE prophylaxis using LMWH (Enoxaparin 40 mg/day). Three levels of eligibility for prophylaxis were examined:
2.a. Restricted: where only patients with strongest risk factors were given prophylaxis (malignancy, especially with chemotherapy, previous history of VTE, some rarer high risk conditions such as inflammatory bowel disease. (~ 25% of all inpatient admissions)
2.b. Intermediate: where patients with strong and moderate risk factors,

Intervention 1: £29
Intervention 2-Restricted : £26
Intervention 2-Intermediate : £30
Intervention 2-Broad :
 £39

Currency & cost year:
Australian dollars presented here as 2014 UK pounds[c]

Cost components incorporated
LMWH prophylaxis
Treatment costs for DVT, PE, PTS and major bleeds
Nursing time
Hospital costs
GP visits
Monitoring

Intervention 1: 0.0004
Intervention 2:
Restricted: 0.0005
Intermediate: 0.0006
Broad: 0.0009

Total DVTs[b] (mean per patient):
Intervention 1: 0.0043
Intervention 2:
Restricted: 0.0025
Intermediate: 0.0024
Broad: 0.0021

Total PEs[b] (mean per patient):
Intervention 1: 0.0023
Intervention 2:
Restricted: 0.0020
Intermediate: 0.0020
Broad: 0.0019

1. No VTE Prophylaxis: dominated
2.a (Restricted eligibility): baseline
2.b. (Intermediate eligibility): extendedly dominated (da)
2.c. (Broad eligibility) vs 2.a. (restricted eligibility): £29,861 per DVT averted (da)

PEs
1. No VTE Prophylaxis: dominated
2.a (Restricted eligibility): baseline
2.b. (Intermediate eligibility): extendedly dominated (da)
2.c. (Broad eligibility) vs 2.a. (restricted eligibility): £170,827 per DVT averted (da)

Death
1. No VTE Prophylaxis: £30,000 per death averted
2.a (Restricted eligibility): baseline
2.b. (Intermediate eligibility): dominated (da)
2.c. (Broad eligibility) vs 2.a. (restricted eligibility): dominated (da)

Analysis of uncertainty:
A range of sensitivity analyses were conducted including changing baseline VTE risk, fatality rate for PE and major bleeding and assumptions regarding VTE risk in non-eligible patients.

such as cardiac or respiratory failure, sepsis or inflammation, are given prophylaxis (~ 40% of all inpatient admissions) 2.c. Broad: where everyone from the intermediate group as well as those satisfying an age criterion (>40 or >60) are given prophylaxis (~80% of all inpatient admissions)

Data sources

Health outcomes: Data on symptomatic DVTs, PEs and major bleeding were based on the results of the PREVENT trial. **Quality-of-life weights:** n/a. **Cost sources:** national unit costs were used and these were obtained from the Medicare Benefits Schedule, Australia and the Department of Health and Ageing, Canberra.

Comments

Source of funding: NR. **Limitations:** Some uncertainty regarding the applicability of resource use and cost data from Australia in 2014 to current NHS context. Discounting was used only for health outcomes and the rate used is different from that recommended in the NICE Reference Case. QALYs are not used as an outcome measure. The model has a short time horizon that covers only the duration of the hospital stay, hence, does not capture long term costs. Only symptomatic events are included in the model. The source of baseline risk and relative treatment effects is based on a single trial and is not reflective of the total body of evidence. The results of the costs and outcomes are not presented as means per patient.

Overall applicability:[b] Partially applicable   **Overall quality**[c] Potentially serious limitations

Abbreviations: CCA: cost-consequence analysis; 95% CI: 95% confidence interval; da: deterministic analysis; DVT: Deep vein thrombosis; ICER: incremental cost-effectiveness ratio; LMWH: low molecular weight heparin; n/a: not applicable; NR: not reported; pa: probabilistic analysis; PE: pulmonary embolism; QALYs: quality-adjusted life years; VTE: venous thromboembolism.
(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.
(b) Calculated by NGC based on 1,458,600 inpatient admissions.
(c) Converted using 2014 purchasing power parity[715]
(d) Directly applicable / Partially applicable / Not applicable
(e) Minor limitations / Potentially serious limitations / Very serious limitations

Study	[Wilbur 2011[1007]]

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Study details	Population & interventions	Costs	Health outcomes	Cost-effectiveness
Economic analysis: CCA (health outcome: DVT [distal or proximal, not progressing to PE], combined toward events (PE, major bleed and death)) **Study design:** probabilistic decision analytic model **Approach to analysis:** Decision tree model to simulate the hospital stay of medical patients with results for cancer patients reported as subgroup analysis. **Perspective:** Canadian institutional (i.e. hospital perspective) **Time horizon:** 7 days **Treatment effect duration:**[a] 7 days **Discounting:** Costs: NA ; Outcomes: NA	**Population:** Hospital adult internal medicine patients. **Cohort settings:** Start age: NR Male: NR **Intervention 1:** UFH (5000 U, twice daily [bid], SC) initiated on day 1 of hospital stay and continued for 7 days. **Intervention 2:** LMWH (enoxaparin 40 mg, once daily [od], administered subcutaneously [SC]) initiated on day 1 of hospital stay and continued for 7 days (mean LOS for internal medicine patient in the institution).	**Total costs (mean per patient):** Intervention 1: £2,892 Intervention 2: £2,896 Incremental (2−1): £4 (95% CI: NR; p=NR) **Cancer subgroup:** **Total costs (mean per patient):** Intervention 1: £2,908 Intervention 2: £2,910 Incremental (2−1): £2 (95% CI: NR; p=NR) **Currency & cost year:** 2009 Canadian dollars (presented here as 2009 UK pounds[b]) **Cost components incorporated:** Only direct medical costs included: -Thromboprophylaxis drug costs -VTE diagnosis - VTE treatment	**True DVT events (mean per patient):** Intervention 1: 0.024 events Intervention 2: 0.021 events Incremental (2−1): - 0.003 events (95% CI: NR; p=NR) **Untoward events (mean per patient):** Intervention 1: 0.0115 events Intervention 2: 0.0102 events Incremental (2−1): - 0.0013 events (95% CI: NR; p=NR) **PE events (mean per patient):** Intervention 1: 0.005 events Intervention 2: 0.004 events Incremental (2−1): - 0.001 events (95% CI: NR; p=NR) **Major bleeding events (mean per patient):**	**ICER (Intervention 2 versus Intervention 1):** £1,116 **per DVT averted** (da) 95% CI: NR £3,726 **per untoward event averted** (da) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NA **Cancer subgroup:** **ICER (Intervention 2 versus Intervention 1):** £287 **per DVT averted** (da) 95% CI: NR £1,037 **per untoward event averted** (da) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NA **Analysis of uncertainty:** One way sensitivity analyses were conducted to examine the robustness of the model results to changes in the following parameters' values:

-pharmacy and nursing time
For administering and preparing the medications
-hospitalisation costs
-costs of treating major bleeding (extended length of stay, treatments and other management costs)

Intervention 1: 0.0005 events
Intervention 2: 0.0002 events
Incremental (2−1):
 - 0.0003 events
(95% CI: NR; p=NR)

Death (mean per patient):
Intervention 1: 0.006 events
Intervention 2: 0.006 events
Incremental (2−1):
 0.000 events
(95% CI: NR; p=NR)

Cancer subgroup:
True DVT events (mean per patient):
Intervention 1: 0.037 events
Intervention 2: 0.031 events
Incremental (2−1): - 0.006 events
(95% CI: NR; p=NR)

Untoward events (mean per patient):
Intervention 1: 0.044

-acquisition cost of LMWH (using the cost of other LMWHs included in the systematic review: dalteparin and nadroparin)
-costs of managing PE and major bleeding
-baseline rate of DVT
-probability of progression to PE in absence of treatment
-assuming alternative LOS

PSA was also conducted, assigning distributions for each model parameter . It was conducted using "untoward events averted as the effectiveness outcome).

The SAs were consistent across the different scenarios considered. None of the SAs were conducted for the cancer subgroup.

events

Intervention 2: 0.037
events

Incremental (2−1): - 0.007
events

(95% CI: NR; p=NR)

**PE events (mean per
patient):**
Intervention 1: 0.007
events

Intervention 2: 0.006
events

Incremental (2−1): - 0.001
events

(95% CI: NR; p=NR)

**Major bleeding events
(mean per patient):**
Intervention 1: 0.0006
events

Intervention 2: 0.0003
events

Incremental (2−1):
 - 0.0003 events

(95% CI: NR; p=NR)

Death (mean per patient):
Intervention 1: 0.006
events

Intervention 2: 0.006

			events	
			Incremental (2−1):	
			0.000 events	
			(95% CI: NR; p=NR)	

Data sources

Health outcomes: Baseline risk for the UFH group and relative treatment effect of LMWH vs UFH for DVT and major bleeding were based on a published review of the literature (Mismetti 2000 [644]) while probabilities of PE and death were sourced from other published papers . Heparin induced thrombocytopenia (HIT), PTS, minor bleeding were not modelled. **Quality-of-life weights:** NA. **Cost sources:** Costs of prophylaxis were obtained from the Vancouver general Hospital Pharmacy. Costs of investigations and tests were obtained from the British Columbia Medical Association Guide to Fees. Nursing and Pharmacy labour costs were based on estimate of time spent in preparation and administration of prophylaxis. The pharmacist wage rate was obtained from the Health Sciences Association of British Columbia while the nurse wage rate was obtained from the British Columbia Nurses' Union. Hospitalisation costs were calculated by multiplying length of stay by the per-diem cost. Costs of treating major bleeding were based on published studies.

Comments

Source of funding: no funding received. **Limitations:** Some uncertainty regarding the applicability of resource use and cost data from Canada in 2009 to current NHS context. The perspective used was that of the institution. QALYs are not used as an outcome measure. The model has a short time horizon that covers only the duration of the hospital stay (7 days), hence, does not capture long term costs and effects. The main outcome reported (untoward events) is a composite outcome measure and its use would underestimate the rate of these events as the occurrence of multiple events is counted as one event. The source of baseline risk and relative treatment effects is slightly outdated. Unit costs are based on both national and local sources and it is not clear if the local sources are reflective of national unit costs. The results of the sensitivity analysis were not reported for the cancer subgroup. **Other:** Investigations to confirm DVT were Doppler ultrasound, examination of the legs, D-Dimer testing and Chest X-ray. Investigations to confirm symptomatic PE are electrocardiogram (ECG) and chest compound tomography (CT) scan with contrast. Treatment strategy for detected VTE would be LMWH and oral anticoagulation with warfarin (initiated at 5 mg orally daily and titrated to international normalised ration (INR) 2-3.

Overall applicability:[(c)] partially applicable **Overall quality**[(d)] potentially serious limitations

Abbreviations: bid: twice daily; CCA: cost-consequences analysis; 95% CI: 95% confidence interval; da: deterministic analysis; DVT: Deep vein thrombosis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); HIT: heparin induced thrombocytopenia; ICER: incremental cost-effectiveness ratio; LMWH: low molecular weight heparin; LOS: length of stay; NA: not applicable; NR: not reported; od: once daily; pa: probabilistic analysis; PE: pulmonary embolism; PTS: post-thrombotic syndrome; QALYs: quality-adjusted life years; SC: subcutaneous; UFH: un-fractionated heparin; VTE: venous thromboembolism.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2009 purchasing power parities[715]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations