COST BURDEN OF VENOUS THROMBOEMBOLISM AND ITS PROPHYLAXIS IN THE UNITED STATES

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Objectives
Venous thromboembolism (VTE) has been the focus of numerous recent healthcare policy changes and initiatives in the United States (US). Varied methods of VTE prophylaxis exist and guideline adherence is low; here the current economic burden of VTE is evaluated and the budget impact of different methods of VTE prophylaxis considered, given their differing efficacy and safety profiles.
Methods
A structured literature search of PubMed was performed, using Medical Subject Headings (MeSH) and title and abstract searches to identify literature specific to VTE and VTE prophylaxis published on or after January 1, 2012. Returned literature were uploaded to *Sourcerer* (Covalence Research) for duplicate detection and title and abstract screening. Screening was performed by two reviewers against pre-defined exclusion criteria. Budget impact analysis was via a Markov model in Microsoft Excel®, including health states of 'no VTE', 'deep vein thrombosis (DVT)', 'pulmonary embolism (PE)', 'DVT and PE', 'death', 'previous VTE', and 'post-thrombotic syndrome'. Alongside this ran a Markov model including 'no bleed', 'minor', 'major', and 'death'.
Results
Searches returned 1,123 articles on efficacy and safety of VTE prophylaxis and 636 articles on healthcare burden. The estimated cost of VTE in the US is $10 billion, with each episode estimated to cost between $9,407 and $28,353 for VTE and $11,486 to $19,901 for PE. Recurrent events incurred reported costs of up to $82,110 in combined inpatient and outpatient costs. Major bleeding related to VTE prophylaxis was also associated with high costs: $10,346 to $28,177. No substantial differences in cost were apparent between prophylaxis with low-molecular-weight heparin and intermittent pneumatic compression (IPC) but decreased bleeding with IPC resulted in IPC being cost saving in certain scenarios.
Conclusions
VTE is a significant burden to healthcare provision in the US. Different methods of prophylaxis do not substantially alter budgets, but IPC may reduce costs.

BACKGROUND

The US Surgeon General identified VTE as a major public health problem [1]

- VTE can be "silent" with the first sign of a problem being mortality [1]
  - It is the leading cause of preventable inpatient death [2]
  - Up to 72% of VTE cases occur after hospital discharge [3]
- Failure to provide prophylaxis to at-risk patients is a medical error [1]
  - Multiple methods of VTE prophylaxis exist including drugs (e.g. heparin) and mechanical methods (e.g. IPC)
  - Little is known about the impact of different VTE prophylaxis methods on healthcare budgets

AIMS

Evaluate the current literature to estimate the US burden of VTE and the budget impact of different prophylaxis methods for healthcare payers using a standard pay for service model for total hip arthroplasty (THA) and total knee arthroplasty (TKA)

METHODS

Literature review

Structured search of PubMed was performed to identify recent publications relating to the incidence and costs of VTE and adverse events (AEs).

- Title and abstract searches and MeSH terms restricted returned hits to those specific to VTE, anticoagulation, prophylaxis, or bleeding published from 2012 onwards
  - Searches were performed on September 21, 2015
  - Duplicates removal and screening was performed by two reviewers using *Sourcerer* (Covalence Research)
  - Title and abstract screening against pre-defined exclusion criteria selected hits that provided cost and/or incidence data

Budget-impact model

Separate Markov models were developed in Microsoft Excel® to simulate the onset and progression of VTE and AEs

- The semi-Markov model for VTE included: 'no VTE', 'DVT', 'PE', 'DVT and PE', 'previous VTE', 'post-thrombotic syndrome (PTS)', 'Fatal VTE', and 'death'
- The AE Markov model included: 'no AE', 'minor bleed', 'major bleed', 'fatal bleed', 'wound infection' and 'heparin-induced thrombocytopenia (HIT)'
  - Flexible Markov model order can assess structural uncertainty
  - Death was consolidated between the two Markov models
  - The AE model only ran during the duration of prophylaxis
- Prophylaxis options included: low-molecular-weight heparin (LMWH), unfractionated heparin, rivaroxaban, apixaban, warfarin, IPC, and no prophylaxis

Base case

A hospital performing 3,500 THA and 4,500 TKA procedures per year in patients with mean characteristics of age 65.9 years, body mass index (BMI) 32.0 kg/m^2, and 41.9% male [4,5]

- Prophylaxis duration was 30 days as per guidelines [5]
  - DVT and PE occurred at a rate of 1.8% and 0.7%, respectively, per 42 days [6]
  - Minor and major bleeds occurred at a rate of 9.9% per 42 days and 1.7% per 11 days, respectively [6,7]
- Event costs were derived from the literature review and adjusted to 2014 USD using the US healthcare-specific PPI
  - Intervention costs and market share were informed by Analy$ource, literature review and current pricing [4,8, 9]
  - A percentage point of market share was moved from LMWH to IPC
- The model time horizon was 1 year with no cost discounting

Sensitivity analyses

Probabilistic analyses evaluated the robustness of results to changes in all input parameters via sampling

- Results from 500 simulations are presented with the median and 95% credible intervals (CrI)
- One-way analysis tested the impact of other event cost options

Table 1. Event costs

Event	USD* per event [Reference]	Value in model, 2014 USD
DVT	9,407 [10] to 28,353 [11]	9,513
PE	11,486 to 19,901 [10]	11,616
DVT and PE	27,909 [12]	36,996
PTS	839 to 3,817 [13]	1,317
HIT	14,387 [14]	17,041
Major bleed	10,346 to 28,177 [15]	17,428 (other), 35,931 (ICH)
Minor bleed	239 [16]	364
Wound infection	7,003 to 25,721 [17]	7,584 (superficial), 27,853 (deep)

DVT, Deep-vein thrombosis; HIT, Heparin-induced thrombocytopenia; ICH, Intracranial hemorrhage; PE, Pulmonary embolism; PTS, Post-thrombotic syndrome. * As per reference, not inflated

RESULTS

Literature review identified 1,123 articles on efficacy and safety of VTE prophylaxis and 636 articles on burden

- After title and abstract screening, 146 efficacy and safety hits and 230 burden hits remained for analysis

Cost of illness

The estimated cost of VTE in the US is $10 billion *per annum* [18]

- Recurrent events were the most costly, with combined inpatient and outpatient costs reaching $82,110 [12]
  - Costs for DVT and PE varied considerably by study (Table 1) and insurance provider
  - Major bleeding related to VTE prophylaxis was also associated with high costs.
- Long-term costs were also high, with PTS associated with an annual burden of $200 million [19]

Budget impact analysis

In the base case, a 1%-point market share change from LMWH to IPC resulted in a cost reduction of $90,779 (Table 2)

- A significant but not substantial saving of $12 per patient year (95% CrI: $9; $14)
- Cost savings were significant (Figure 1) although the change in DVT (95% CrI: -0.63; 0.38) and PE (-0.36; 0.96) were not

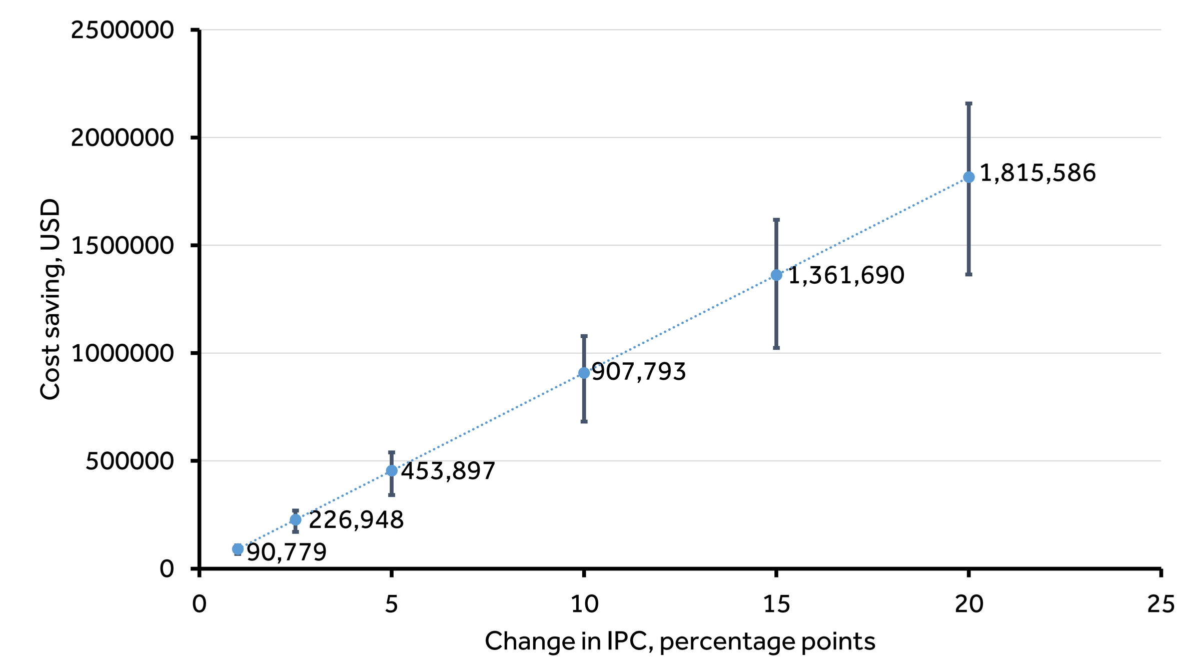
Table 2. Base case results

Outcomes at 1 year	Current care	LMWH -1%, IPC +1%
Total cost, USD	15,449,024	15,358,245
Cost per patient year, USD	2,045	2,033
DVT, N patients	216	216
PE, N patients	79	79
Major bleed, N patients	285	284
Minor bleed, N patients	448	445

DVT, Deep-vein thrombosis; IPC, Intermittent pneumatic compression; LMWH, Low-molecular weight heparin; PE, Pulmonary embolism;

- Significant reductions in minor (95% CrI: -3.98; -1.88) and major (-0.90; -0.08) bleeds were apparent when using IPC in place of LMWH
- To the nearest $1000, each percentage-point increase in IPC market share reduced costs compared with LMWH by $91,000 (Figure 1) and no prophylaxis by $42,000
- Cost of prophylaxis was the largest cost driver, but if LMWH was at no cost, the total cost saving with IPC was $23,339 (95% CrI: $809; $40,448) driven by reduced AEs (bleeding)
  - The breakeven point was determined to be when IPC cost $357 more than LMWH per patient per 30 days of prophylaxis
- Changing AE costs did not significantly alter model findings
  - If bleeding events incurred no cost IPC was associated with a saving of $79,954 (95% CrI: $59,354; $95,789)
  - Bleeds had a larger impact on costs than did VTE events
- Modeling only significant difference between prophylaxis options, the cost saving with IPC was significant at $88,085

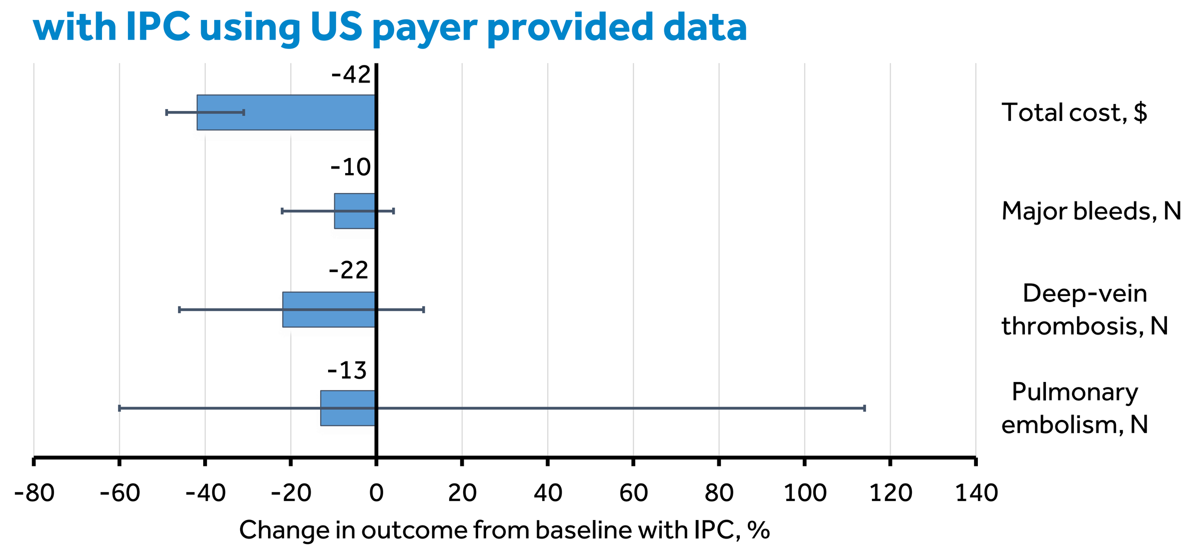
Figure 1. Estimated cost saving and 95% credible intervals per %-point change in market share from LMWH to IPC



Scenario analyses

- Using market share and prophylaxis cost data provided by a US payer, transferring all patients to IPC would reduce total costs by $7.8 million, a 42% reduction (Figure 2) [20]
- In an analysis using German cost and incidence data, IPC reduced total costs by EUR 17,733 in the base case (95% CrI: EUR 12,780; EUR 21,840) [9†]

Figure 2. Percentage change (95% CrI) in model outcomes with IPC using US payer provided data



CONCLUSIONS

- VTE is a significant burden to the US healthcare system
- Small changes in the methods of prophylaxis chosen will not substantially alter budgets
- Increased use of IPC for VTE prophylaxis can reduce the cost of care for payers in the US
- Significant reduction in bleeding events with IPC increases patient safety and leads to cost savings

ACKNOWLEDGMENTS

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