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, 2011. Recurrent events were considered. Sources were restricted to the US and to studies in English. Specific terms were included in the search algorithm (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’ pre-existing 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 634 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 for VTE and $36,996 for PE. Recurrent events were defined as the combination of both patients with and without VTE reoccurrence. Significant reduction in bleeding events with IPC increases the estimated cost saving with IPC in some cost scenarios.

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 Sourcerc (Covalence Research)
- Title and abstract screening against pre-defined exclusion criteria selected articles 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.

- 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 TKAs procedures per year in patients with mean characteristics of age 65.9 years, body mass index (BMI) 32.0 kg/m², and 41.9% male (4.6%

- Prophylaxis duration was 30 days as per guidelines
- DVT and PE occurred at a rate of 1.8% and 0.7%, respectively, per 42 days
- Minor and major bleeds occurred at a rate of 9.9% per 42 days and 1.7% per 11 days, respectively

- 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 AnalySource, literature review and current pricing
- A percentage point of market share was moved from LMWH to IPC

- Model time horizon was 1 year with no cost discounting

Significance 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)

Table 1. Event costs

<table>
<thead>
<tr>
<th>Event</th>
<th>USD* per event</th>
<th>Value in model, 2014 USD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>11,486 to 19,901 [10]</td>
<td>11,166</td>
</tr>
<tr>
<td>DVT and PE</td>
<td>27,909 [12]</td>
<td>36,996</td>
</tr>
<tr>
<td>PTS</td>
<td>839 to 1,317 [13]</td>
<td>1,317</td>
</tr>
<tr>
<td>HIT</td>
<td>14,387 [14]</td>
<td>17,041</td>
</tr>
<tr>
<td>Major bleed</td>
<td>10,346 to 28,177 [15]</td>
<td>17,428 (other), 35,911 (ICH)</td>
</tr>
<tr>
<td>Minor bleed</td>
<td>239 [16]</td>
<td>364</td>
</tr>
<tr>
<td>Wound infection</td>
<td>7,003 to 25,721 [17]</td>
<td>7,584 (superficial), 27,853 (deep)</td>
</tr>
</tbody>
</table>

Table 2. Base case results

<table>
<thead>
<tr>
<th>Outcomes at 1 year</th>
<th>Current care</th>
<th>LMWH–15%, IPC+1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cost, USD</td>
<td>15,449,024</td>
<td>15,358,245</td>
</tr>
<tr>
<td>Cost per patient, USD</td>
<td>2,045</td>
<td>2,033</td>
</tr>
<tr>
<td>DVT, N patients</td>
<td>216</td>
<td>216</td>
</tr>
<tr>
<td>PE, N patients</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>Major bleed, N patients</td>
<td>285</td>
<td>284</td>
</tr>
<tr>
<td>Minor bleed, N patients</td>
<td>448</td>
<td>445</td>
</tr>
</tbody>
</table>

Table 3. Results from 2014 and 2015 with LMWH and IPC

- 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: $890; $400,448 driven by reduced AEs (bleeding)
- The breakeven point was determined to be when IPC cost $537 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

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]

**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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**REFERENCES**

**WARNING**
This document contains patient medical information. It is intended for healthcare professionals and should not be used to make clinical decisions. Further analysis and interpretation may be necessary. Always consult a healthcare professional for medical advice.