Background

- Anticoagulation is essential for deep vein thrombosis (DVT) and pulmonary embolism (PE) prevention following total knee arthroplasty (TKA).
- Prolonging the duration of anticoagulation post-TKA can significantly reduce DVT and PE risks.
- Clinicians must weigh the risks of DVT and PE against those of excessive anticoagulation, including hemorrhage and prosthetic joint infection (PJI).

Methods

- Model Structure (Figure 1): State-transition Monte-Carlo computer simulation model (TreeAge Pro®) following subjects for one year post-TKA, tracking clinical and economic outcomes of TKA and anticoagulation therapy.
- Subjects transition between the following major health states post-TKA:
  - DVT, PE, PJI, hemorrhage, no postoperative complications

Input Data (Table 1):

- Published literature, RedBook Online®, Medicare Fee Schedules
- Each anticoagulant associated with unique cost, efficacy, and bleeding risk
- Each complication associated with unique cost, quality of life, and mortality

Anticoagulation Strategies:

- Anticoagulants considered:
  - Fondaparinux, Rivaroxaban, Low molecular weight heparin (LMWH), Warfarin, Aspirin
  - Duration of post-TKA anticoagulation: Standard duration (14-day) or Prolonged duration (35-day)

Outcomes:

- Proportion of first post-operative year spent in each health state
- Incremental cost-effectiveness ratio (ICER)
- Increase in costs (dollars)
- Increase in health benefits (QALYs)

Figure 1. Model Structure

Table 1. Select Input Parameters

<table>
<thead>
<tr>
<th>Anticoagulation Characteristics</th>
<th>Daily Cost</th>
<th>RR DVT</th>
<th>RR Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fondaparinux</td>
<td>$431</td>
<td>0.08</td>
<td>2.21</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>$8</td>
<td>0.12</td>
<td>2.12</td>
</tr>
<tr>
<td>LMWH</td>
<td>$371</td>
<td>0.20</td>
<td>1.23</td>
</tr>
<tr>
<td>Warfarin</td>
<td>$6/35</td>
<td>0.36</td>
<td>1.21</td>
</tr>
<tr>
<td>Aspirin</td>
<td>$1</td>
<td>0.69</td>
<td>1.0</td>
</tr>
</tbody>
</table>

LMWH: Low molecular weight heparin
1 Inclusive cost of injection administration ($26)
2 Week 1/Weeks 2+: inclusive cost of monitoring

Table 2. Cost-effectiveness of anticoagulation strategies after TKA

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cost</th>
<th>QALY</th>
<th>ICER</th>
<th>DVT</th>
<th>Bleed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged Rivaroxaban</td>
<td>$3,279</td>
<td>0.7328</td>
<td>Cost Saving</td>
<td>18.0%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Prolonged Warfarin</td>
<td>$3,291</td>
<td>0.7325</td>
<td>Cost Saving</td>
<td>21.9%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Standard Rivaroxaban</td>
<td>$3,416</td>
<td>0.7322</td>
<td>Cost Saving</td>
<td>22.8%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Standard Warfarin</td>
<td>$3,551</td>
<td>0.7319</td>
<td>Reference</td>
<td>25.6%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Prolonged Asprin</td>
<td>$3,689</td>
<td>0.7315</td>
<td>Dominated</td>
<td>25.7%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Standard Asprin</td>
<td>$3,777</td>
<td>0.7312</td>
<td>Dominated</td>
<td>28.4%</td>
<td>3.4%</td>
</tr>
<tr>
<td>No prophylaxis</td>
<td>$3,869</td>
<td>0.7262</td>
<td>Dominated</td>
<td>32.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Standard LMWH</td>
<td>$3,898</td>
<td>0.7321</td>
<td>Dominated</td>
<td>23.9%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Standard Fondaparinux</td>
<td>$3,932</td>
<td>0.7323</td>
<td>$977,100</td>
<td>22.3%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Prolonged LMWH</td>
<td>$4,375</td>
<td>0.7326</td>
<td>Dominated</td>
<td>19.5%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Prolonged Fondaparinux</td>
<td>$4,529</td>
<td>0.7328</td>
<td>$1,085,600</td>
<td>17.3%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

Figure 1. Cost-Effectiveness Acceptability Curve

Results

Objective

- Evaluate the cost-effectiveness of prolonged (35-day) and standard (14-day) duration anticoagulation therapy following TKA

Figure 3. Distribution of Costs in the First Postoperative Year for Prolonged Strategies

Figure 4. Proportion of the First Postoperative Year Spent in Each Health State for Prolonged Strategies

Cost-Saving

- 5% for Prolonged Rivaroxaban
- 3% for Prolonged Warfarin
- 3% for Prolonged Asprin
- 5% for Standard Rivaroxaban

Limitations

- There are sparse data on continued efficacy of anticoagulants in extended prophylactic period
- We assumed, in the base case, that aspirin did not increase the risk of bleeding. We addressed the uncertainty in this parameter in sensitivity analyses.

Conclusions

- Prolonged therapies increase QALY’s compared to standard duration durations, supporting the extension of anticoagulation post-TKA.
- Prolonged prophylaxis with warfarin and rivaroxaban emerged as cost-effective strategies.
- As prolonged rivaroxaban and warfarin are comparable from a cost-effectiveness standpoint, patient preferences can help inform the choice of the appropriate postoperative anticoagulation strategy.

Anticoagulation Strategy

- Rivaroxaban
- Fondaparinux
- LMWH
- Aspirin
- Warfarin

Table 2. Cost-effectiveness of anticoagulation strategies after TKA

- Prolonged Rivaroxaban: $3,279, QALY 0.7328, ICER 18.0%
- Prolonged Warfarin: $3,291, QALY 0.7325, ICER 21.9%
- Standard Rivaroxaban: $3,416, QALY 0.7322, ICER 22.8%
- Standard Warfarin: $3,551, QALY 0.7319, ICER 25.6%
- Prolonged Asprin: $3,689, QALY 0.7315, ICER 25.7%
- Standard Asprin: $3,777, QALY 0.7312, ICER 28.4%
- No prophylaxis: $3,869, QALY 0.7262, ICER 32.1%
- Standard LMWH: $3,898, QALY 0.7321, ICER 23.9%
- Standard Fondaparinux: $3,932, QALY 0.7323, ICER 22.3%
- Prolonged LMWH: $4,375, QALY 0.7326, ICER 19.5%
- Prolonged Fondaparinux: $4,529, QALY 0.7328, ICER 17.3%

Cost Savings

- $1,085,600 for Prolonged Rivaroxaban
- $3,898 for Prolonged Warfarin
- $3,777 for Standard Asprin
- $3,689 for Prolonged LMWH
- $3,551 for Prolonged Fondaparinux

Quality-Adjusted Life Years

- 80% for Prolonged Rivaroxaban
- 78% for Prolonged Warfarin
- 23% for Standard Rivaroxaban
- 80% for Prolonged LMWH
- 80% for Prolonged Fondaparinux