Cost-Effectiveness Analysis of Drug Eluting Stents (DES) Compared with Bare Metal Stents (BMS) Based on an Ontario Field Evaluation

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RAILONELT
- Stents cost province of Ontario $14 million in 01/02
- Volume projected to increase by 37% over 5 years
- Health Canada approved DES in 2002/03
- Sirolimus (Cypher®) & Paclitaxel (Taxus®)
- Stents are less expensive
- Up-take of DES in US approximately 90%
- Therefore, DES represent a major cost concern due to higher cost and volume projections
- However, RCTs indicate DES have a lower rate of restenosis (offsetting re-do-PCI procedure costs)
- Treatment effect may be greater for specific sub-groups
- ‘Real world’ effectiveness of DES uncertain
- ‘Real world’ cost-effectiveness of DES uncertain

OBJECTIVES
- Conduct a systematic literature review of effectiveness of DES vs. BMS.
- Construct a field evaluation to collect ‘real world’ rates of revascularization in the province.
- Conduct an interim analysis on a subset of patients with at least 9 months of follow-up recruited into the field evaluation.
- Conduct a decision analytic model to evaluate the cost-effectiveness of DES versus BMS.
- Estimate the budget impact for Ontario.

METHODS

Literature Search
- Databases searched:
  - MEDLINE, EMBASE, Cumulative index to nursing & allied health literature (CINAHL), Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and Cochrane Central Register of Controlled Trials (CENTRAL)
- 1st search to December 2004; updated in 2005
- Randomized trials only
- English language studies only since 1990

Economic Evaluation
- Determine cost-effectiveness of DES vs. BMS from field evaluation data and literature
- Model structure
  - 1 year frame
  - Decision analytic model
  - Costs
    - Initial stent costs
  - Revascularization costs – stent and procedure
  - Outcomes
    - Revascularizations averted
    - QALY's gained
  - Perspective: Ontario MOH

RESULTS

Table 1. Unadjusted Revascularization Rates (all patients)

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>All Patients</th>
<th>Non-Diabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI without stent</td>
<td>5 (1.12%)</td>
<td>2 (1.22%)</td>
<td>3 (1.21%)</td>
</tr>
<tr>
<td>TVR-PCI with stent</td>
<td>16 (3.57%)</td>
<td>10 (4.51%)</td>
<td>6 (5.25%)</td>
</tr>
<tr>
<td>Total Stent</td>
<td>37 (8.26%)</td>
<td>21 (9.86%)</td>
<td>16 (9.70%)</td>
</tr>
</tbody>
</table>

Table 2. Multivariate Weibull 1-year TVRa Rates in Non-MII Patients, by Lesion Characteristic and Diabetes Status

<table>
<thead>
<tr>
<th>Lesion Characteristic</th>
<th>Non-Diabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long &amp; narrow lesions</td>
<td>14.0%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Long &amp; complex lesions</td>
<td>18.6%</td>
<td>7.9%</td>
</tr>
<tr>
<td>Long &amp; complex lesions</td>
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<td>6.9%</td>
</tr>
</tbody>
</table>

Table 3. Multivariate Weibull 1-year TVRa Rates in Post-MII Patients, by Lesion Characteristic and Diabetes Status

<table>
<thead>
<tr>
<th>Lesion Characteristic</th>
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Figure 1. Basic structure of the decision tree

- By cohort and by stent type, 5 endpoints
  - Target lesion revascularization (TLR)
  - PCI with stent
  - Target vessel revascularization (TVR)
  - PCI with stent
  - Target vessel revascularization adjusted (TVRa)
  - TVR with stent, all PCI without stent, CABG
  - All revascularization procedures
  - CABG, PCI with stent, PCI without stent
  - Mortality (all causes)

Unadjusted vs Adjusted Rates
- The event rates in patients receiving DES are similar to the rates reported in the RCT's.
- The event rates for patients receiving BMS are substantially lower than that reported in RCT’s.
- Therefore the difference in revascularization rates between DES and BMS were lower in field evaluation than reported in clinical trials.
- Can be due to imbalances (observational bias)
- Multivariate regression analysis used to adjust for differences in baseline characteristics
- Age, gender, LAAD, stent length, stent size, lesion severity, multiple vessel disease, angina severity

Figure 2. Literature review and evaluation of suitable articles for meta-analysis

- 11 Primary study reports – 9 unique studies
- Randomized controlled trials
- Randomized trials only
- MEDLINE, EMBASE, Cumulative index to nursing & allied health literature (CINAHL)
- Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and Cochrane Central Register of Controlled Trials (CENTRAL)
- Excluded Articles
  - Registry Study
  - Case Series
  - Non-randomized trials
  - Registry Study
  - Case Series

Figure 3. Patients included in the Interim Analysis

- (n = 9,103 with minimum 9 months of follow-up)
- Clinical outcomes (n = 14)
- Clinical outcomes (n = 14)
- OSR (high surgical risk)
- OSR (low surgical risk)

Figure 4. Cost-Effectiveness Acceptability Curves

- High cost-effectiveness of ($/revascularization avoided or <$/QALY gained) even in most favorable group
- Based on interim results, OHTAC recommended DES for patients with at least 2 of the following:
  - Diabetes, long lesions, narrow lesions
  - Without this controlled diffusion, costs of stents in the province were estimated to approach $57 million in F06/07 (compared to $35 million with current recommendations)
  - OHTAC’s recommendation for controlled diffusion will result in reduced expenditures on stents to the government of $22 million in F06/07
  - Future cost savings will depend on the price of stents (which have been decreasing)

Discussion
- Results from the field evaluation did not demonstrate the same relative difference in revascularization rates as seen in the RCT literature
- There are a number of possible explanations:
  - Real-world patients vs. clinical trial patients (all Ontario patients (diverse) & all lesion types)
  - Newer generation of BMS than in earlier trials
  - Differences in use of post PCI pharmacotherapy
  - Protocol-driven revascularizations
  - Selection bias for DES & BMS use. Analyses may not control for all of this (uncontrolled nature of registry data)
- Final report with even larger sample (n > 20,000) and longer follow-up period due out Q4/06