ECONOMIC EVALUATION OF TREATMENT STRATEGIES FOR LATE-PRESENTATION ACUTE ISCHEMIC STROKE

JULIAN NAM (@JNAM27)
DARIA O’REILLY

ACUTE ISCHEMIC STROKE

- Stroke: leading cause of disability
- 80% of all strokes are of ischemic type
- Reduced blood and oxygen to the brain
- Occlusion of a cerebral artery
TREATMENT

- **BEST MEDICAL TREATMENT (BMT)**
  - General supportive care
  - Most widely received treatment

- **INTRAVENOUS THROMBOLYSIS (IVT)**
  - Intravenous tissue plasminogen activator (tPA)
  - Approved window: <3 hours after SO
  - Recommended treatment window: <4.5 hours after SO

TREATMENT CONT’D

- **INTRA-ARTERIAL THROMBOLYSIS (IAT)**
  - Intra-arterial administration of tPA via endovascular device
  - Recommended up to 6 hrs after SO in middle cerebral artery occlusions

- **MECHANICAL THROMBECTOMY (MT)**
  - Physical removal of thrombus via endovascular device
  - Approved to “remove blood clots from the brain in patients experiencing an ischemic stroke”
LATE-PRESENTATION

FOUR TREATMENTS
- Recommended strategies, and/or
- Widely used

UNCERTAIN ECONOMIC BENEFIT:
- No evaluation for all treatments in late time window

OBJECTIVE

Cost-effectiveness of intravenous thrombolysis (IVT), intra-arterial thrombolysis (IAT) and mechanical thrombectomy (MT) vs. best medical treatment (BMT) in late-presentation acute ischemic stroke patients
DECISION ANALYTIC MODEL (1/2)

**DESIGN:**
- Probabilistic decision tree for year 1
- Probabilistic Markov model for long term

**TIME HORIZON:**
- Lifetime

**PERSPECTIVE:**
- Third-party health care payer

**DISCOUNT:**
- 3% discount rate

DECISION ANALYTIC MODEL (2/2)

**POPULATION (BASE CASE):**
- 65 year old with ischemic stroke
- Late presentation: 3-4.5 hours from symptom onset

**INTERVENTION:**
- Best medical treatment (BMT)
- Intravenous thrombolysis (IVT)
- Intra-arterial thrombolysis (IAT)
- Mechanical thrombectomy (MT)

**OUTCOMES:**
- Effects: quality-adjusted life years (QALYs)
- Costs: healthcare resource cost (2011 Canadian dollars)
HEALTH STATES

- MODIFIED RANKIN SCALE (mRS)
  - Level of disability in daily activities
  - Ranges from 0 to 6
    - mRS 0 indicates no symptoms at all
    - mRS 6 indicates death

- HEALTH STATES:
  - Independent in daily activities (mRS 0, 1, 2)
  - Dependent in daily activities (mRS 3, 4, 5)
  - Death (mRS 6)
  - Recurrent stroke
PARAMETER SOURCES (1/2)

- **90-DAY MORALITY, 90-DAY DISABILITY IN DAILY ACTIVITIES, HEMORRHAGIC COMPLICATION**
  - IVT: Pooled analysis of 7 RCTs
  - IAT: Pooled analysis of 2 RCTs
  - MT: Observational study

- **DISCHARGE DESTINATION**
  - Ischemic stroke survivors from the Ontario Stroke Registry

- **QUALITY-ADJUSTED LIFE YEARS**
  - Ischemic stroke survivors from a UK registry

PARAMETER SOURCES (2/2)

- **LONG-TERM SURVIVAL**
  - Ischemic stroke survivors from the Saskatchewan Health administrative database

- **HEALTHCARE COSTS**
  - Ontario Case Costing Initiative
  - Hamilton ischemic stroke survivors
90-DAY MORTALITY, 90-DAY DISABILITY, HEMORRHAGIC COMPLICATION

- 90-DAY INDEPENDENCE (mRS 0,1,2) given survival
  - IVT: RR 1.10 (95%CI: 1.01 to 1.20)
  - IAT: RR 1.39 (95%CI: 1.02 to 1.89)
  - MT: RR 1.48 (95%CI: 0.94 to 2.31)

- 90-DAY DEATH
  - IVT: RR 0.99 (95%CI: 0.74 to 1.32)
  - IAT: RR 0.85 (95%CI: 0.58 to 1.57)
  - MT: RR 0.97 (95%CI: 0.59 to 1.59)

UTILITIES

Each mRS is important

- INDEPENDENT and DEPENDENT: costs/utilities weighted by proportion of patients with component scores

<table>
<thead>
<tr>
<th></th>
<th>BMT</th>
<th>IVT</th>
<th>IAT</th>
<th>MT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Utility</td>
<td>0.52</td>
<td>0.55</td>
<td>0.64</td>
<td>0.64</td>
</tr>
</tbody>
</table>

* Component scores not available (use of IAT or BMT weights have no effect on decision outcomes)
HEALTHCARE COSTS

Cost

Discharge destination
(home w/services, home w/o services, LTC, rehab)

Health state
(Independent/Dependent)

Treatment (IVT/BMT)

COSTS

Annual resource use cost

<table>
<thead>
<tr>
<th>Resource</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMT initial hospitalization</td>
<td>$11,456</td>
</tr>
<tr>
<td>IVT initial hospitalization</td>
<td>$12,812</td>
</tr>
<tr>
<td>IAT initial hospitalization</td>
<td>$20,689</td>
</tr>
<tr>
<td>MT initial hospitalization</td>
<td>$18,123</td>
</tr>
<tr>
<td>Rehab</td>
<td>$15,913</td>
</tr>
<tr>
<td>Home with services, Independent</td>
<td>$2,930</td>
</tr>
<tr>
<td>Home with services, Dependent</td>
<td>$26,058</td>
</tr>
<tr>
<td>Long term care (Ayr)</td>
<td>$36,082</td>
</tr>
</tbody>
</table>

$0 $20,000 $40,000
RESULTS: BASE CASE

- MT dominates
- IAT, IVT still effective

<table>
<thead>
<tr>
<th></th>
<th>BMT</th>
<th>Incr. Δ IVT</th>
<th>Incr. Δ IAT</th>
<th>Incr. Δ MT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life Years</td>
<td>7.85</td>
<td>0.00</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>QALYs</td>
<td>3.95</td>
<td>0.22</td>
<td>0.81</td>
<td>0.93</td>
</tr>
<tr>
<td>Cost</td>
<td>$82,108</td>
<td>-$2,277</td>
<td>-$10,655</td>
<td>-$17,130</td>
</tr>
</tbody>
</table>

RESULTS: COST-EFFECTIVENESS PLANE

INCREMENTAL COSTS VS. INCREMENTAL QALYS
RESULTS: COST-EFFECTIVENESS ACCEPTABILITY CURVE

PROBABILITY OF COST-EFFECTIVENESS VS. WTP THRESHOLD

LIMITATION

-Observational data on efficacy of MT

-Can explore the expected value of perfect information (EVPPI) of clinical inputs for MT:
  -At a WTP of $50,000: EVPPI per patient = $18,048

-There still remains uncertainty about the underlying point estimate
  -Can be tested with a threshold analysis
  -High-quality efficacy data needed
CONCLUSIONS

- Balance of effects and costs favour endovascular approaches such as MT, IAT
- Decision uncertainty around the best endovascular treatment
- Next step: collect higher quality data for MT
- Next step: explain sources of uncertainty

ACKNOWLEDGEMENTS

Daria O'Reilly, Ron Goeree, Feng Xie, Gord Blackhouse, Jean-Eric Tarride and the rest of PATH