Risky Business – Decision Making in Health Care with Economic Uncertainty

A Case Study of Parameter Uncertainty

Stephen Goodall
PBAC guidelines – sensitivity analysis

- Conduct univariate analysis
- Compare with base case
- Conduct multivariate analysis
- Discuss sensitivity to change

- 2/350 pages dedicated to sensitivity analysis
Aim

- To provide 2 case studies
- Demonstrate how estimating parameter uncertainty can inform decision-making
  - One-way
  - Multivariate
  - Threshold
  - Probabilistic sensitivity analysis
Case Study 1

- Radiofrequency Ablation for Barrett’s Oesophagus with dysplasia

- Focus on low grade dysplasia
Barrett’s Oesophagus

- Increased risk of oesophageal cancer
  - 5 year survival of less than 10%
  - HG/Cancer symptoms: persistent heartburn, difficult or painful swallowing, recurrent vomiting, weight loss
  - LG: asymptomatic

Intestinal Metaplasia

Low Grade Dysplasia

High grade dysplasia

Oesophageal Adenocarcinoma

University of Technology Sydney
Treatments – Low grade dysplasia

- **Surveillance**
  - Endoscopy every 6 months with biopsies of BO tissue

- **Radio Frequency Ablation + surveillance**
  - 3 treatments of RFA
  - Surveillance every 6 months for 5 years then once a year
Effectiveness (complete eradication)

- 1 RCT - Shaheen et al (2009)
- RFA vs. sham procedure
  - One year success rate
    - RFA: 90.5%
    - Sham: 22.7%
# Cost-effectiveness – Base case

<table>
<thead>
<tr>
<th></th>
<th>Total Cost</th>
<th>Total QALYs</th>
<th>Incremental Cost</th>
<th>Incremental QALYs</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance</td>
<td>$13,225</td>
<td>10.049</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RFA</td>
<td>$23,400</td>
<td>10.178</td>
<td>$10,175</td>
<td>0.129</td>
<td>$78,975</td>
</tr>
</tbody>
</table>
Sensitivity analysis - one-way

- Test each parameter one at a time
  - Usually CIs or plausible range
  - E.g. Effectiveness of RFA
    - i.e. transition probability - low grade to no dysplasia
    - 90.5% (41% - 100%)

<table>
<thead>
<tr>
<th>Effectiveness of RFA</th>
<th>1 year success rate</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>90.5%</td>
<td>~$80,000/QALY</td>
</tr>
<tr>
<td>High 95% Confidence interval</td>
<td>100%</td>
<td>~$70,000/QALY</td>
</tr>
<tr>
<td>Low 95% Confidence interval</td>
<td>41%</td>
<td>~$340,000/QALY</td>
</tr>
</tbody>
</table>
Graphical presentation of multiple one-way analysis - Tornado Plot

ICER ($/QALY)

- Low Grade to No Dysplasia (100%, 41%)
- Low Grade to Cancer (0.016, 0.006)
- Cost of RFA (-50%, +100%)
- No Dysplasia to Low Grade (0.01, 0.078)
- Cost of Cancer (+25%, -25%)
- Low Grade to High Grade (0.05, 0.013)
- High Grade to No Dysplasia (100%, 32%)
- Death from Cancer (50%, 15%)
- High Grade to Low Grade (0.0405, 0.0889)
- No Dysplasia to High Grade (0.0028, 0.083)
- Utility rates (1, 1, 1, 0.5)
Threshold Analysis

- Model sensitive to cancer progression rate (low grade to cancer)
  - One-way SA - ICER ($45,000/QALY to $300,000/QALY)

- Threshold analysis
  - Set threshold and determine when parameter yields cost-effective outcome
  - E.g. at $50,000/QALY - Rate of LG to cancer > 1.5%

- Meta-analysis:
  - 0.5% of all BO patients progress to cancer
  - Wani et al (2009)
    - LG to cancer: 1.7%

- Cohort studies:
  - LGD to Cancer
    - Bhat (2011): 1.4%
    - De Jonge (2010): 0.39%
    - Sharma (2006): 0.6%
Threshold - LG to Cancer

Higher rates = more cost-effective
$50.000/QALY = 0.015
Probabilistic Sensitivity Analysis (PSA)

Probabilities

ln(RR)

Costs

1-Utilities

Probabilities

ln(RR)

Costs

1-Utilities

Low Grade Dysplasia

High Grade Dysplasia

Cancer

No Dysplasia

Death

Costs and QALYs
Probabilistic Sensitivity Analysis

All points show a combination of incremental costs and outcomes of intervention A relative to intervention B.

Baseline = $23,000/QALY

Low
($20k)

Mid
($50k)

High
(80k)
ICE Scatterplot of RFA vs. Surveillance

$50,000/QALY
Cost-effectiveness acceptability curves (CEAC)
Interpreting CEACs

Radiofrequency ablation versus surveillance in patients with low grade Barrett’s Oesophagus

Acceptability Curve

- Probability Cost-Effective
- Willingness to Pay

- Surveillance
- RFA
Conclusions - MSAC

- On the basis of its high cost and uncertainty of clinical benefit due to uncertainty of progression rate from Barrett’s Oesophagus with low grade dysplasia (LGD) to oesophageal cancer, MSAC does not support public funding for radiofrequency ablation (RFA) in the treatment of Barrett’s Oesophagus with LGD.

Case Study 2

- Falls prevention strategies in NSW

Diagram:
- Increased risk of falling
- More unstable on feet
- Fall or stumble
- Loss of confidence
- Fear of falling
- Decreased body strength
- Reduced home or community duties
Markov Model

- Low Risk Faller
- Medium Risk Faller
- High Risk Faller
- Long Term Care
- Dead
Decision pathways

Low Risk Faller → Medium Risk Faller → High Risk Faller → Long Term Care → Dead

Discharged home to community
- Discharged to residential care
  - Residential aged care
    - p_discharged_residential
    - Death
    - p_death
  - p_residential_aged_care
    - Medium Risk

Hospitalised
- p_hospitalised
  - Discharged to residential care
    - Residential aged care
      - p_discharged_residential
      - Death
      - p_death
    - p_residential_aged_care
      - Medium Risk

Emergency attendance
- p_emergency
  - Discharged to residential care
    - Residential aged care
      - p_discharged_residential
      - Death
      - p_death
    - p_residential_aged_care
      - Medium Risk

Fall
- p_falling
  - Other medical attendance
    - p_other_medical
      - Residential aged care
        - p_residential_aged_care
        - Death
        - p_death
      - p_nursing_home
        - Low Risk
      - p_death
  - p_fall
    - Residential aged care
      - p_residential_aged_care
      - Death
      - p_death
    - p_nursing_home
      - Low Risk
    - p_death

Community
- p_comunt
  - Residential aged care
    - p_residential_aged_care
    - Death
    - p_death
  - p_nursing_home
    - Low Risk
    - p_death

Not Injured
- p_not_injured
  - Residential aged care
    - p_residential_aged_care
    - Death
    - p_death
  - p_nursing_home
    - Low Risk
    - p_death

Death
- p_death
Model Assumptions – Duration of costs & Benefits (i.e. structural uncertainty)

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Model 1 C=1, B=∞</th>
<th>Model 2 C=1, B=1</th>
<th>Model 3 C=∞, B=∞</th>
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<tbody>
<tr>
<td>Exercise</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Tai Chi</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Home Hazard</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Medication Withdrawal</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Expedited Cataract Surgery</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Cardiac Pacing</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Multiple Interventions</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>Multi-factorial Interventions</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tbody>
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**Model 1**
- Cost of intervention incurred only in first year
- Benefits last for length of model

**Model 2**
- Cost of intervention incurred only in the first year
- Benefits last only for first year

**Model 3**
- Cost of intervention incurred each year
- Benefits last for length of model
## Results QALYs - Exercise

- **Cost per QALY – 75 year olds (10 years)**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Avg Cost</th>
<th>QALYs</th>
<th>ICER</th>
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<tbody>
<tr>
<td>No Intervention</td>
<td>$3,697</td>
<td>4.649</td>
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<tr>
<td>Home exercise</td>
<td>$4,684</td>
<td>4.658</td>
<td>$103,268</td>
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<td>Group exercise</td>
<td>$4,158</td>
<td>4.655</td>
<td>$69,501</td>
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<tr>
<td>“Stepping On” program</td>
<td>$4,387</td>
<td>4.657</td>
<td>$79,220</td>
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Tornado Diagram – exercise

- No fear of falling
- Cost of intervention ($282, $1126)
- Effectiveness (0.67, 0.87)
- Age (85, 65)
- Fear of Falling (0.06, 0.03)
- Fall rate factor (1.4, 1)
- Utility of fracture (0.072, 0.28)
- Probability of falling (uniform across risk group)

ICER

$0 $50,000 $100,000 $150,000 $200,000
Multi-way SA
- cost, effectiveness and age

<table>
<thead>
<tr>
<th>65 year olds - 10 years</th>
<th>Cost of Intervention</th>
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<tr>
<td></td>
<td>$250</td>
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<tr>
<td>0.67</td>
<td>$34,859</td>
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<tr>
<td>0.72</td>
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<td>0.76</td>
<td>$50,862</td>
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<td>0.82</td>
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<td>0.87</td>
<td>$98,545</td>
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<td>0.67</td>
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<td>$38,579</td>
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<td>0.76</td>
<td>$57,566</td>
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<table>
<thead>
<tr>
<th>85 year olds - 10 years</th>
<th>Cost of Intervention</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>$250</td>
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<tr>
<td>0.67</td>
<td>cost saving</td>
</tr>
<tr>
<td>0.72</td>
<td>cost saving</td>
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<td>0.76</td>
<td>cost saving</td>
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<tr>
<td>0.82</td>
<td>$694</td>
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<tr>
<td>0.87</td>
<td>$11,448</td>
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</table>
Threshold Sensitivity Analysis

Net Monetary Benefit (wtp=60000.) Sensitivity Analysis on age and intervention_rr and intervention_cost

Baseline RR Group Exercise = 0.76 (0.67, 0.87)
When is PSA useful? - multiple interventions

CEAC - falls prevention interventions in residents of aged care facilities

Acceptability Curve

- No Intervention
- Vitamin D
- Medication Review
- Multi-factorial
- Hip protectors
Final thought on PSA

- Do decision makers use PSA?
  - NICE only recommend drugs with a >40% certainty of being cost-effective. Adalsteinsson et al (2013)

- Confidence in the base case ICER?
  - Base-case $70k/QALY
  - PSA - 15% probability of being cost-effective at $60k/QALY

- Why not use all the data/information?

- Choice of distributions is arbitrary?
  - Limit choice of appropriate distributions

- Not always useful? – neither are seat belts
Summary

- **Aim of sensitivity analysis**
  - Estimate the uncertainty in economic models
  - Identify key drivers (what influences the model results)
  - Identify areas of further research

- **Different methods**
  - One-way & Multi-way should always be conducted
  - Threshold can be informative to decision makers
    - particularly when there is uncertainty regarding a key variable
  - PSA uses the full information available
    - Can provide extra confidence in base case ICER
    - Requires good quality data
    - Useful when comparing several interventions
References

  

  