Module 4 – Economic evaluation, uncertainty & modelling
Centre for Health Policy
Melbourne School of Population and Global Health

Purpose of economic evaluation

- Inform decisions!
  - Is the intervention cost-effective?
  - How does it compare to other interventions?
- Helps translate study results into information for:
  - Decision makers at your hospital
  - Evidence base within your field
  - Government funding agencies

Incremental cost effectiveness ratio (ICER)

- How? Bring costs and benefits together to allow comparisons

\[
\text{ICER} = \frac{\text{Costs}_I - \text{Costs}_C}{\text{Outcomes}_I - \text{Outcomes}_C}
\]

- Incremental; common outcome measures
- CEA \rightarrow maximisation of health outcomes within given funding/budgets
**Costs**

- **Incremental cost effectiveness ratio (ICER)**
  - Within study costs
  - Outside study costs
  - Discounting
  - Inflating

**Outcomes**

- **Within study outcomes**
- **Outside study outcomes**
- **Modelling**
  - Discounting
  - Inflating
- **Skewed data**

**Uncertainty?**

\[
\text{ICER} = \frac{\text{Costs}_C - \text{Costs}_C}{\text{Outcomes}_C - \text{Outcomes}_C}
\]

**Clinical**

- Typically primary outcomes
- Consider translation to other outcomes?

**Economic**

- Standard metric is the Quality Adjusted Life Year (QALY)

**Key for studies? Perspective differences**

- Clinical 'success' at point in time
- Economics interested in gains over time

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**QoL ≠ QALY**

- QoL has no time dimension; QALY adds an explicit temporal dimension: \( \text{QALY} = \text{QoL} \times \text{duration} \)

- QoL score of 0.8 for 2 years = 1.6 QALYs
- QoL score of 0.5 for 4 years = 2.0 QALYs

**Utility instruments**

- **Clinical**
- **Economic (QALY)**

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**Outcomes**

**Point of intervention**

- **Comparator**
- **Study seeks to show this clinical effect**
- **QoL gain is the area between the curves**

**Economics is interested in gain over time**
Cost data

- Likely to be skewed
- Wide confidence intervals
- Missing versus zero values

<table>
<thead>
<tr>
<th></th>
<th>Perindopril-indapamide</th>
<th>Placebo/standard practice</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs</td>
<td>$21,001</td>
<td>$20,499</td>
<td>$502</td>
</tr>
<tr>
<td>Years of life</td>
<td>4.17</td>
<td>4.14</td>
<td>0.03</td>
</tr>
<tr>
<td>Eq-5D</td>
<td>0.8</td>
<td>0.8</td>
<td>-</td>
</tr>
<tr>
<td>QALY</td>
<td>3.33</td>
<td>3.31</td>
<td>0.02</td>
</tr>
</tbody>
</table>

CEA= $502/0.03 = $16,733 per life year saved
CUA= $502/0.02 = $25,100 per QALY saved

Key for studies: Could we estimate this prior to study?

Cost effectiveness analysis

Within study results: the ADVANCE study

Key for studies? Costs unlikely to be powered (uncertainty around costs)

Economic Modelling

Why is it necessary?
Clinical studies are limited in scope and duration: they do not contain all the information required by decision makers

- Need to extrapolate beyond study follow-up period
- Need to generalise from one setting/population to another
- Need to link between intermediate and final outcomes (transform)
- Need to evaluate uncertainty

Extrapolation: costs

- Within study versus long-term costs

Extrapolation: outcomes

Economics is interested in gain over time
QALY gain is the area between the curves
QALY gain continues post study
Point of Intervention
End of study
Time

QoL

Comparator
Extrapolation data adjustments

- Discounting (time preferences)
  Both costs and outcomes

- Inflation (changes in prices over time)
  - $1.75 in 1986
  - $5.30 in 2016

  Costs

Cost effectiveness analysis

<table>
<thead>
<tr>
<th></th>
<th>Within study</th>
<th>Within study + modelling</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs</td>
<td>$502</td>
<td>$502</td>
<td>-</td>
</tr>
<tr>
<td>Years of life saved</td>
<td>0.03</td>
<td>0.05</td>
<td>-40%</td>
</tr>
<tr>
<td>QALYs saved</td>
<td>0.02</td>
<td>0.03</td>
<td>-33%</td>
</tr>
<tr>
<td>$/years of life saved</td>
<td>$16,733</td>
<td>$10,040</td>
<td>67%</td>
</tr>
<tr>
<td>$/QALY saved</td>
<td>$25,100</td>
<td>$16,733</td>
<td>50%</td>
</tr>
</tbody>
</table>

- Key for study: within study results may underestimate cost effectiveness
  - Consider how you expect the outcomes to vary

Generalisability

- An RCT finds folic acid during pregnancy improves birth outcomes
- Should the Department of Health fund a folic acid program to all pregnant women?
- What do we need to know?
  - How many pregnant women each year?
- Key for studies?
  - Design your study sample to be representative or measure how it is different
  - Consider power for sub-cohorts

Transformation

- An RCT is used to highlight how a new intervention can improve the glycemic control in type 1 diabetes patients
- What are the long-term implications of this?
  - Simulation model transforms change in risk factor (e.g. blood glucose) to change in outcomes (e.g. fewer strokes)
- Key for studies?
  - Final outcomes could be immeasurable within study: do models exist to transform your intermediate outcomes to final outcomes?

Evaluating uncertainty

- Studies aim to reduce uncertainty
  - Is the intervention effective?
- Typically focus on randomisation and sample size (parameter uncertainty)
- But still much uncertainty
  - Structural/model
  - Methodological
  - Combinations of primary and secondary data
Evaluating uncertainty

- Modelling can help systematically evaluate uncertainty: sensitivity analysis

- Key for studies?
  - Many areas of uncertainty
  - Not just parameter uncertainty!
  - Try to capture rather than ignore uncertainty
  - Identify likely sources of uncertainty
  - Use modelling to help evaluate the impact of uncertainty

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Georges E.P. Box

Evaluating uncertainty
Demystifying modelling

- Different types of modelling?
  - Survival analysis
  - Decision analysis, Markov
  - Microsimulation

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>QALYs</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.6</td>
<td>$10,000</td>
</tr>
<tr>
<td>B</td>
<td>0.8</td>
<td>$30,000</td>
</tr>
</tbody>
</table>

Model population:
e.g. cohort 16-40yrs

Probability A e.g. 0.3
Probability B e.g. 0.7

Bringing it all together

- Analysis and manipulation of costs
  - Skewed data
  - Inflation, discounting
- Analysis of outcomes
  - Clinical data
  - Calculation of QALYs
  - Discounting
- Out-of-study costs and outcomes?
  - Modelling

Interpreting economic evaluations

- How can economic evaluations be interpreted?
- How do they feed into decisions?
- What exactly are we trying to show?
- Key for studies? How will the study influence a decision? Start with the end in mind

Interpreting economic evaluations

Graphing costs and effects

Costs

QALYs

Costs

QALYs

Cost-effectiveness plane

NE

NW

SW

NW

NE

SW

Costs

Effects

New treatment more costly

Existing treatment dominates

New treatment less effective

New treatment less costly

New treatment more effective but more costly

New treatment less costly but less effective

Existing treatment dominates

New treatment more effective but more costly

New treatment less costly

New treatment less costly
Decision rules for CEA

- **Recommend**
  - If new intervention dominates
- **Reject**
  - If new intervention is dominated
- Develop a decision rule for NE & SW quadrants
  - Compare to established threshold
- Key for studies? Where do you expect the intervention to lie? What’s the ‘pitch’?

How do I know if it is cost effective?

- What is the maximum amount society is willing to pay for an extra unit of health gain?
- Varies across countries
  - Australia $40K-$70K per life year
  - UK, NICE states £20-30K per QALY
  - US $50,000 per QALY as a minimum

Considerations with thresholds

- In practice in Australia, thresholds vary
  - Medical versus lifestyle interventions
  - Treatment versus screening objectives
  - Child versus adult target populations

Probabilistic sensitivity analysis

- Cost-effectiveness plane


Probabilistic sensitivity analysis

- Cost-effectiveness plane

- Cost-effectiveness plane

$12,500/QALY

$25,000/QALY

**Probabilistic sensitivity analysis**

**Cost-effectiveness plane**

- $50,000/QALY


**Cost-effectiveness plane**

- $100,000/QALY


**Cost-acceptability curve**

- Key for studies: acceptability curves help to inform decisions


**Guidelines for reporting**

- Guidelines available to apply across the research cycle
  - Informing protocol development
  - Citing in funding applications
  - Using in practice
  - Reporting results

- Key for studies: helps guide smooth path for acceptance

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**Incremental cost-effectiveness ratio (ICER)**

- Costs\(_i\) / Outcomes\(_i\) - Costs\(_C\) / Outcomes\(_C\)
Key points for studies

• Differences between clinical and economic outcomes
  – Plan follow-up measurements
• Within study results might underestimate cost-effectiveness
  – Think about how outcomes might vary
• Many areas of uncertainty
  – Don’t ignore, but evaluate
• Study should help to inform a decision
  – Estimate cost-effectiveness prior to study
  – Use guidelines and standard economic evaluation methods

Other contributions from economics

Informing decisions

• Economics is essentially a tool to help make decisions, of which there are plenty in study design:
  – Economics of recruitment
  – Economics of follow-up timing
  – Economics of site selection
  – Economics of duration of study
  – Etc!

Follow-up scheduling example

• Measurements only after stabilisation led to 10% bias in QALY gain estimations

Efficiency of clinical studies example

• Current grant application to investigate drivers of recruitment and cost. What makes for more efficient studies?
  – Location
  – Accreditation
  – Ethics
  – Type of centre
  – Staff expertise and experience
  – Centre experience in running studies
  – Scale
  – Clinician engagement
• Fundamentally, economics considers marginal (incremental) costs and benefits

• Key for studies? Does the marginal benefit outweigh the marginal cost?
  – An extra follow-up point?
  – A larger sample?
  – Including more outcome measures?
  – Including different sites?