Using economic modelling to contribute to the prioritisation and design and clinical trials: ready for prime time

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Overview

• The role of economic evaluation in supporting decisions
• What are the implications for how we prioritise and design evidence generation?
• Are economic methods being used to inform research funding?
• Expected value of information methods – the right tool?
• What other methods can help?
Context

• Growing role for economic evaluation, although prominence varies
• National vs. local impact of economic evaluation
• Policy impact likely to grow
  – Tighter budgets for health care
  – Pressure of transparency
• Continuous need to show value from R&D
• Timely to reflect on how economic evaluation is being used with trials
Role of economic evaluation

**DECISIONS**
Are the health effects of new interventions greater than the health decrements relating to the displacement of services associated with any additional cost?

- Against all comparators
- Using all relevant evidence
- For defined populations, sub-populations and context
- Over appropriate time horizons
Iterative nature of evaluation

- Uncertainty cannot be eliminated
- Undertake research until its value < cost
Implications for new evidence generation

• Need to understand existing practice and evidence
  – All relevant existing evidence
  – Comparators
  – Role of new technology/intervention
  – Population and sub-groups

• Understand cost effectiveness of new intervention given existing evidence

• Understand uncertainty in cost-effectiveness (decision uncertainty)

• Determine priority research (and appropriate design) to reduce uncertainty in cost-effectiveness
How much of this is done?

- Systematic review of existing evidence
  - New intervention: Usual
  - Comparators: Rare

- Synthesis of existing clinical evidence: Sometimes

- Cost-effectiveness modelling: Very rare

- Inform trial design using economic modelling: Very rare
Some examples...

- Systematic review of existing evidence
  - New intervention: √ √ √ √
  - Comparators: X X X X X

- Synthesis of existing clinical evidence: X X X X X

- Cost-effectiveness modelling: X X X X X

- Inform trial design using economic modelling: X X X X X


REFLUX: Minimal access surgery compared with medical therapy in chronic reflux disease. *BMJ* 2008; 337;a2664


Do we have the tools to do it properly?

• What do we need?
  – Quantification of decision uncertainty
  – Quantification of costs of uncertainty
  – Cost of research
  – Marginal costs and benefits of specific studies

• Expected value of information (EVI)
  – Expected value of perfect information
  – Expected value of sample information

• Increasing number of examples in published literature

• Often requested as part of HTA Programme secondary research
Calculating EVPI

<table>
<thead>
<tr>
<th></th>
<th>Treatment A</th>
<th>Treatment B</th>
<th>Optimal choice</th>
<th>Maximum Net benefit</th>
<th>Opportunity Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iteration 1</td>
<td>9</td>
<td>12</td>
<td>B</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Iteration 2</td>
<td>12</td>
<td>10</td>
<td>A</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Iteration 3</td>
<td>14</td>
<td>20</td>
<td>B</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Iteration 4</td>
<td>11</td>
<td>10</td>
<td>A</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Iteration 5</td>
<td>14</td>
<td>13</td>
<td>A</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Expectation</td>
<td>12</td>
<td>13</td>
<td></td>
<td>13.8</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Current information = 13
Perfect information = 13.8
EVPI = 13.8 - 13 = 0.8

\[ EVPI = \mathbb{E}_\theta \max_j \text{NB}(j, \theta) - \max_j \mathbb{E}_\theta \text{NB}(j, \theta) \]
# Examples of EVI having impact

## Table 3: Interventions in each maternal risk group with a probability of being cost effective of at least 1%*

<table>
<thead>
<tr>
<th>Maternal risk groups in hierarchical order</th>
<th>% of total population</th>
<th>Intervention</th>
<th>Probability of being cost effective</th>
<th>Expected value of information per year in UK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preterm deliveries (&lt;37 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Planned caesarean section</td>
<td>0.80</td>
<td>IV antibiotic</td>
<td>0.5870</td>
<td>£5 281 333</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.4120</td>
<td></td>
</tr>
<tr>
<td>2. Previous baby with GBS</td>
<td>0.01</td>
<td>IV antibiotic</td>
<td>0.8590</td>
<td>£7 820</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.1370</td>
<td></td>
</tr>
<tr>
<td>3. Positive urine or vaginal swab for GBS in current pregnancy</td>
<td>0.44</td>
<td>IV antibiotic</td>
<td>0.9730</td>
<td>£81 600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.0178</td>
<td></td>
</tr>
<tr>
<td>4. Fever ≥38.0°C in labour</td>
<td>0.25</td>
<td>IV antibiotic</td>
<td>0.7800</td>
<td>£539 467</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.2160</td>
<td></td>
</tr>
<tr>
<td>5. Rupture of membranes before onset of labour</td>
<td>2.41</td>
<td>IV antibiotic</td>
<td>0.5800</td>
<td>£12 806 667</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.4190</td>
<td></td>
</tr>
<tr>
<td>6. Spontaneous labour (membrane rupture &lt;2 hours before or after onset of labour)</td>
<td>3.43</td>
<td>IV antibiotic</td>
<td>0.8590</td>
<td>£4 193 333</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.1370</td>
<td></td>
</tr>
<tr>
<td><strong>Term deliveries (≥37 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Planned caesarean section</td>
<td>7.99</td>
<td>Oral antibiotic</td>
<td>0.6720</td>
<td>£1 586 667</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV antibiotic</td>
<td>0.3270</td>
<td></td>
</tr>
<tr>
<td>8. Previous baby with GBS</td>
<td>0.08</td>
<td>IV antibiotic</td>
<td>0.6060</td>
<td>£30 600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.3930</td>
<td></td>
</tr>
</tbody>
</table>

*Colbourn et al. BMJ 2007;335;655*
Fewer examples of expected value of sample information - EECP

Routine use of EVI methods

New methods of analysing cost effectiveness

Value of information analyses must be integrated into the process of commissioning primary research

Interest in whether health interventions are value for money as well as effective has meant that the term cost effectiveness\(^1\) is commonly used (and sometimes misused) in the clinical literature. Consequently, methods for determining cost effectiveness have been refined, especially techniques for synthesising evidence and representing uncertainty in the results of such evaluations. Techniques such as multi-parameter evidence synthesis\(^2\) and value of information analysis\(^3\) are now routinely integrated into cost effectiveness studies, especially health technology

This contrasts with the Cochrane review approach, which typically uses only randomised evidence to assess a single treatment comparison.

In addition, a probabilistic analysis of uncertainty in the parameters of the model allows a full assessment of the implication of the estimated uncertainty for the decision. This means the analysis can answer two fundamental questions relating to the choice between the strategies evaluated. Firstly, on the basis of the existing evidence, what is the preferred course of action? Secondly, should additional information
Why is EVI not getting used to guide research funding decisions?

• Limited use of EVI by research funders/ commissioners
  – 2003 pilot work by HTA Programme*
  – Little experience with key concepts
  – No scope to interact with the modelling
  – Challenge of making it practical

• Limited use in trial proposals
  – How many health economists understand and use EVI?
  – Challenge of communication and training
  – How influential are economists in developing proposals
  – Does modelling and EVI need additional funding?

* Claxton et al. Health Technology Assessment 2004; Vol. 8: No. 31
Claxton and Sculpher. Pharmacoeconomics 2006; 24 (11): 1055-1068
Are there alternatives to EVI?

- Currently little economic analysis is used to help commissioners prioritise research or assess designs
- Conventional power calculations available for economics
  - Inconsistent with the needs of decision makers
  - Not used!
- Contextual information about prioritisation: decision uncertainty rather than burden of illness
- Resource allocation issues not always a priority
- Are trial endpoints relevant to resource allocation decisions?
- Would the minimum ‘detectable’ effect size result in cost-effectiveness?
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