Trial Based Economic Evaluation: Just Another Piece Of Evidence

Claxton K
Department of Economics and Centre for Health Economics,
University of York, UK
Is the purpose of evaluation to inform decisions?

• What are the decisions?
• What is required?
• Which evidence is relevant?
• Does uncertainty matter?
• What is the role of trials?
• Are there any dangers?
What decisions?

• Given existing evidence:
  – Which interventions/strategies should be implemented?
  – For which patient/population groups?
  – For what type of indications/settings?

• Is further evidence required to support decisions?
  – What type of evidence
  – What type of studies
  – For which patient groups
  – How much evidence

• Delay implementation until the evidence is available?
So what’s required?

– Joint distribution of cost and outcomes
– For all alternative interventions/strategies
– Explore the full range of clinical policies
– For range of patient groups
– In the relevant decision context
– Over an appropriate time horizon
Should we consider all the evidence?

• Should social decision making consider all the evidence of relative effect?
  – Central tenant of EBM
  – Expected cost and outcomes
  – Characterisation of the uncertainty

• Should we compare all alternative interventions or only the selection included in a particular study?

• Should we also consider all the evidence for other parameters?

• Should we consider both direct and indirect evidence for all parameters?
Direct and indirect evidence?

- Synthesis 1 and 2
- But compare all interventions?
  - Pair wise comparisons?
  - Use all the information
  - Estimate joint posterior LOR with correlations

### Alternative interventions

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
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<tbody>
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Direct and indirect evidence?

- Estimates of parameter values
- Uncertainty surrounding estimates
- Correlations between parameters
Does decision uncertainty matter?

- Is an assessment of the consequences of decision uncertainty necessary for rational (expected value) decision making?
  - Is a characterisation of decision uncertainty a prerequisite for an assessment (formal or informal) of its consequences?
  - Does this require a synthesis of all evidence from a variety of sources?
## Some examples from NICE

### Implications for research prioritisation

<table>
<thead>
<tr>
<th>Case Study</th>
<th>Patient Group</th>
<th>Population EVPI</th>
<th>EVPI for parameters</th>
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<tbody>
<tr>
<td><strong>AMD Screening</strong></td>
<td>Visual acuity 20/40, Visual acuity 20/80</td>
<td>£6.2m, £15.3m</td>
<td>Quality of life with and without PDT (£3,370,000 for 20/40)</td>
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<td><strong>Glycoprotein IIb/IIIa</strong></td>
<td>Acute treatment following non-ST-elevation acute coronary syndrome (scenario 2)</td>
<td>£171m</td>
<td>Relative risk of death for non acute PCI for GPA as medical management and for Clopidogrel (£85,041,000, and £68,137,000 respectively)</td>
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<td><strong>Clopidogrel and dipyridamole for secondary prevention</strong></td>
<td>Stroke, Transient Ischaemic Attack, Myocardial Infarction, Peripheral Arterial Disease (scenario 2)</td>
<td>£865m, £250m, £710m, £240m</td>
<td>Relative risks of vascular and non vascular death (£780m for ASA-MR-dipridamole compared to clopidogrel in the stroke subgroup)</td>
</tr>
<tr>
<td><strong>Neurominidase inhibitors</strong></td>
<td>Otherwise healthy adults not at elevated risk of complications</td>
<td>£66.7m</td>
<td>Quality of life with influenza, the effect of oselatimivir and amantadine (£44.3m, £0.43m and £0.23m respectively)</td>
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<td><strong>Liquid Based Cytology</strong></td>
<td>Women aged 18 to 64 years (scenario 3)</td>
<td>£20m</td>
<td>Specificity (£3.6m)</td>
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<tr>
<td><strong>Disease modifying therapies for multiple sclerosis</strong></td>
<td>Relapsing remitting and primary progressive multiple sclerosis (scenario 2)</td>
<td>£86.2m</td>
<td>Relative risk of progression for copaxone, Betaferon and rebif (22mg) (£14m, £13.6m and £7m respectively) Also the cost of care, costs of relapse and quality of life (£10m, £7m and £6m respectively)</td>
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Can any single study provide a basis for decision making?

- Should we adopt a technology?
- Is further evidence required?

- When would a trial be sufficient basis
  - Trial follow-up and time horizon identical
  - All relevant comparators included as arms
  - Patients and practice relevant to decision-making context
  - All parameters estimated
  - Only source of evidence for all parameters
So what is the role of trials?

• As measurement
  – Particularly parameters subject to selection bias
  – Input to the synthesis of all evidence

• Implications for design
  – Useful for synthesis
  – Pragmatic trials (what is exchangeable)?

• Implications for reporting of evaluations
  – ICERs and certainly CEACs make little sense
  – Value of information without synthesis makes no sense
Do we need economic trials?

- Is Peto right? It's an empirical question

Value of a trial updating all parameters
Do we need economic trials?

- Is Peto right? It's an empirical question

Value of a portfolio of studies

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<tr>
<th>Sample size (n)</th>
<th>Expected net benefit of sample information</th>
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<tr>
<td></td>
<td>PIP</td>
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<td></td>
<td>RSD, PHZ</td>
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<td>UPA</td>
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Why trial based evaluation?

• Historical dominance of frequentist analysis
  – Probability is the relative frequency of repeated events
  – Traditional Inferential rules

• Fully Bayesian decision theoretic analysis
  – Priors based on synthesis of accumulated evidence
  – Specification of the loss function (decision framework)
Leon Trotsky, Preface to The History of the Russian Revolution

- Entirely exceptional conditions, independent of the will of persons or parties, are necessary in order to tear off the fetters of conservatism and bring the masses to insurrection.

- The masses go into revolution not with a preprepared plan of social reconstruction, but with a sharp feeling that they cannot endure the old regime.

Leon Trotsky, Preface to The History of the Russian Revolution