Discrete Event Simulation or Markov Model: War of The Worlds or Expanding the Galaxy?

Mark Sculpher, PhD

Professor of Health Economics
University of York, UK

ISPOR - 11th Annual European Congress, Athens, 2008
Discrete Event Simulation or Markov Model: Why Build a Rocket when a Bicycle will do?

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Why do we model?

• To inform decisions about resource allocation
• Therefore models should deliver:
  – Expected costs and health effects
  – For all options
  – Relating to appropriate population and sub-populations
  – Based on full range of existing evidence
  – Quantification of decision uncertainty
  – Valuation of further research
• In a timely manner to support decisions
Approximations are unavoidable in modelling

“Remember that all models are wrong; the practical question is how wrong do they have to be to not be useful.”* 

The search for ‘absolute accuracy’:
- Adds complexity
- Imposes costs (evidence gathering, computation time)
- Complicates communication
- Need to justify in terms of better decisions

## Managing complexity in cost-effectiveness analysis

<table>
<thead>
<tr>
<th>Analytical issue</th>
<th>The ideal</th>
<th>The pragmatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choice of comparators</td>
<td>All existing ways of managing the relevant patient group</td>
<td>Most widely used; those with a reasonable chance of being cost-effective</td>
</tr>
<tr>
<td>Evidence gathering</td>
<td>Exhaustive search for all sources of evidence for every parameter in the model</td>
<td>Reproducible search; comprehensively related to importance of parameter</td>
</tr>
</tbody>
</table>
Managing complexities in model structure

• **What’s the ideal?**
A model structure able to reflect every potential effect of alternative interventions, and exactly capture every feasible prognostic implication of those effects for every type of patient

• **What are the implications?**
Huge number of parameters to estimate from available evidence imposing very high search and computation costs

• **What’s sufficient?**
A model capturing the major characteristics of a disease and intervention, providing guidance on the adoption and research decisions and able to reflect the robustness of the decisions to added complexity
An example
Modelling adjuvant treatment for early cancer

Remission → Recurrence → Non-cancer deaths

Remission (local rec) → Cancer deaths

Remission (regional rec)

Remission (distant rec)
Where might we want to add complexity?

<table>
<thead>
<tr>
<th>Issue</th>
<th>Modelling response</th>
<th>Evidence?</th>
<th>DES?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline characteristics affect prognosis</td>
<td>Make relevant parameters conditional on baseline characteristics</td>
<td>Parameters by sub-group</td>
<td>No</td>
</tr>
<tr>
<td>Rate of 1\textsuperscript{st} recurrence varies with time</td>
<td>Incorporate time dependent transition probabilities</td>
<td>Rates by time</td>
<td>No</td>
</tr>
<tr>
<td>Side effects of treatment</td>
<td>Are they prognostic? Are the effects additive or multiplicative with cancer</td>
<td>Additional parameters</td>
<td>Possibly</td>
</tr>
<tr>
<td>Post recurrence prognosis exhibits time dependencies and/or heterogeneity</td>
<td>Wrap up as mean prognosis; add additional states</td>
<td>Additional parameters</td>
<td>Possibly</td>
</tr>
</tbody>
</table>
Implications of moving to a DES

- Evidence
  - Need risk of mortality/future cancer events as a function of time from recurrence and/or characteristics at recurrence
  - Mean values plus uncertainty
  - Will this vary by treatment?

- Computational
  - In non-linear models, need two levels of simulation to estimate expected costs and effects
  - Two levels required to quantify decision uncertainty (PSA)
  - Multiple levels of simulation to implement value of information methods
  - Potentially millions of simulations

- Will the adoption and research decisions be influenced by added complexity?
Evidence on DES versus cohort models

Pragmatic way forward?

• All analyses should reflect nature of decision problem, available evidence and requirements of decision making
• Compelling case to start simple (typically cohort)
• What are the marginal costs and benefits of adding complexity in evidence?
• Marginal effects: will added complexity alter decisions?
• *Prima facie* case DES for some decision problems:
  – Build two model structures
  – Do deterministic results differ markedly and importantly?
  – If so, move to DES for uncertainty and sub-group analysis
  – If not, stay with cohort for uncertainty and sub-group analysis