A framework for addressing structural uncertainty in health economic decision models

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Health economic decision-making

- Decision by health service provider whether to fund an intervention (e.g. NICE for UK NHS)
- Taken on the basis of expected long-term benefits and costs compared to existing policies

New intervention cost-effective if

\[
\frac{E(\text{Cost}_{\text{new}} - \text{Cost}_{\text{old}})}{E(\text{QALY}_{\text{new}} - \text{QALY}_{\text{old}})} < \lambda
\]

\(\lambda\) = maximum amount ”willing to pay” for a QALY
Also determine decision uncertainty / need for further research.
Models to estimate costs and effects

1. OUT OF HOSPITAL
2. HOSPITAL (cardiac arrhythmia)
3. HOSPITAL (other cardiac)
4. HOSPITAL (other non-cardiac)
5. HOSPITAL (ICD maintenance)
6. HOSPITAL (ICD replacement)
7. HOSPITAL (AAD side-effects)
8. DEAD

- Commonly **Markov models** for clinical history
- Each state / event associated with a cost or detriment to quality of life
- Combine **all relevant evidence** on disease and treatment – randomised trials → meta-analyses, observational data, national registries...

(Example: cost-effectiveness of implantable defibrillators for cardiac arrhythmia)
Standard procedure for economic modelling

- Choose states to represent important events
- Identify the parameters of the model
  - transition rates between states
  - cost and quality of life for each state
- Identify how these parameters vary
  - between patients and through time
- Estimate parameters from data or expert belief
- Account for ensuing parameter uncertainty probabilistically:

Prior distributions (from data/belief) → model parameters → Monte Carlo simulation → Posterior expected costs / effects
Standard procedure for economic modelling

- Choose states to represent important events
  - Which are relevant to the decision?
- Identify the parameters of the model
  - transition rates between states
  - cost and quality of life for each state
- Identify how these parameters vary
  - between patients and through time
  - What covariates? What time-dependence?
- Estimate parameters from data or expert belief
  Which data are relevant? What if no data?
- Account for ensuing parameter uncertainty probabilistically

But what should be modelled?

*Structural* uncertainty / model uncertainty
Cost-effectiveness often presented for “best case” assumptions . . .

- underestimates uncertainty – may be biased

often alongside alternative scenarios

- with little indication of plausibility of each one
Accounting for structural uncertainty informally

Cost-effectiveness often presented for “best case” assumptions . . .

▶ understates uncertainty – may be biased

often alongside alternative scenarios

▶ with little indication of plausibility of each one

Improve practice – express structural uncertainty in a formal probabilistic way using

▶ statistical model averaging, or

▶ expert elicitation
Framework for addressing structural uncertainty

1. Assign distributions to model parameters, where clear how to do so.
2. Define global model with parameters defining structures (§2).
3. Classify structural parameters: any published data to estimate them?
4. Perform PSA to estimate outputs for single model (or scenarios).
5. For all structural parameters with data:
   - Define sub-models with these parameters omitted (for each scenario if needed).
6. Evaluate fit of each sub-model and global model (§3.1-3.2).
7. Clear best-fitting model? (§3.1)
8. YES: Perform PSA to estimate outputs for best-fitting model.
9. NO: Any remaining structural uncertainty?
10. YES: Define global model with parameters defining structures (§2).
11. NO: For all structural parameters with no data:
   - Any reliable expert knowledge about the parameters?
   - NO: Continue with separate scenarios defined by plausible parameter values.
   - YES: Obtain distribution from expert elicitation for use in PSA (§4).
12. Any structural parameters remaining?
13. YES: Perform PSA to estimate outputs for single model (or scenarios).
14. NO: Results the same under all models?
15. YES: Present PSA outputs for best-fitting model.
16. NO: Average over models costs and effects from PSA (§3.3).
Setting up the model

- **Set up and parameterise model**
- **Expand model** to encompass structural uncertainties
  - Include as many states / events as might affect the decision
  - Allow parameters to vary with as many covariates as possible

Problem...
Setting up the model

- **Set up and parameterise model**
- **Expand model** to encompass structural uncertainties
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  - Allow parameters to vary with as many covariates as possible

**Problem...**

no data / not enough data to inform some parameters
Two possible causes of hospital admission, or combined cause?
No data on relative incidence of causes

Choice between model structures == uncertainty about parameters in bigger model
 Obtaining information with no published data

Sometimes **no published data** to inform a parameter

- Example: will treatment effect persist after trial follow-up?
- use **expert elicitation** to obtain a distribution representing belief
- If no reliable expert belief
  - present results to decision-maker under different plausible scenarios
- Assess value of performing further research (**value of information** methods)
Sometimes weak data to inform some parameters

- Example – is there a treatment effect on some event?
- Have imprecise estimate of the effect from a small sample.
  - Leave effect out of the model (may give bias)?
  - ... Or leave it in the model (may lose precision)

Instead of picking one (best-fitting) model – account for model uncertainty
Obtaining information from weak data

For all structural parameters with data:

- Define sub-models with these parameters omitted (for each scenario if needed).

Evaluate fit of each sub-model and global model (§3.1-3.2)

- Clear best-fitting model? (§3.1)
  - NO: Perform PSA to estimate outputs for each sub-model and global model.
  - YES: Perform PSA to estimate outputs for best-fitting model.

- Results the same under all models?
  - YES: Present PSA outputs for best-fitting model.
  - NO: Average over models costs and effects from PSA (§3.3).

Big statistical literature on model choice / model comparison / model uncertainty

- Discrete: Fit finite set of models
  - Model averaging using weights related to fit
- Continuous: One flexible model including all possibilities
  - Priors chosen for good predictive ability
  - e.g. shrinkage priors, Bayesian nonparametrics
Two surgical techniques for repairing abdominal aortic aneurysm (AAA): EVAR / open repair (Jackson et al. 2010)

- Choice of surgery affects short-term post-operative mortality
- Uncertainty: does it also affect long-term AAA mortality?
- HR 5.84 (0.70, 48.50) from 6 (EVAR) versus 1 (open) AAA deaths over 3 years – strong enough evidence to include HR?
- AIC for models with / without effect → weight of 0.7 for model with effect
- Average expected costs and benefits with / without effect →

<table>
<thead>
<tr>
<th></th>
<th>Probability EVAR cost-effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>with effect</td>
<td>0.08</td>
</tr>
<tr>
<td>without effect</td>
<td>0.38</td>
</tr>
<tr>
<td>model average</td>
<td>0.17</td>
</tr>
</tbody>
</table>
General framework for model uncertainty

Express all modelling uncertainties as parameters in an enlarged model – include everything that might affect the decision.

▶ Data available to inform parameters?
  ▶ use statistical methods e.g. model averaging
▶ Expert judgement available?
  ▶ elicit probability distributions for parameters.
▶ Allows framework to establish benefit of further research on particular parameters
▶ Often no information to judge plausibility of assumptions, e.g. about extrapolations into future (as in climate modelling!)
  ▶ compare potential scenarios
