

# Risky business: decision making in healthcare with economic modelling uncertainty

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## Issues for Discussion

- What are the problems with uncertainty?
- How to deal pragmatically with uncertainty?
- What impacts does uncertainty have on decision-making?

## Background to the Issue

- Uncertainty is a one of the main challenges facing healthcare decision makers when assessing economic models
- Implications of uncertainty are:
  - Decision makers may make a “wrong” decision
  - If they had definitive information their decision may be different

## Decision-maker example of a decision not to recommend

Cladribine, tablet, 10 mg, Movectro®  Merck Serono Australia Pty Ltd  Major submission	Multiple sclerosis	Section 100 listing for the initial and continuing treatment of relapsing – remitting multiple sclerosis (RRMS) initiated by a neurologist, in an ambulatory patient who has experienced at least two documented attacks of neurological dysfunction, believed to be due to multiple sclerosis in the preceding two years who meets certain criteria.	The PBAC rejected the submission because of use of an inappropriate comparator, uncertain clinical benefit and uncertain and unacceptable cost effectiveness in comparison with the appropriate comparator. The appropriate main comparator is interferon beta, the most commonly used first line treatment for multiple sclerosis.
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<http://www.pbs.gov.au/pbs/industry/listing/elements/pbac-meetings/pbac-outcomes>

## Risk of wrong decisions

### Opportunity costs

- Not approved when should have:
  - Some people miss out on getting access to a medicine that will improve their health?
- Approved when should have rejected
  - Cost of paying for an ineffective treatment
  - Price is too high for the benefits?
    - Impacts on budget that could have been spent more effectively on other goods / services

## Uncertain clinical benefit

- Often evident by wide confidence intervals around effect size
    - Small sample size?
  - Duration of clinical trial “too short” to assess true benefits
  - No direct comparative evidence on effects or safety
    - Need indirect comparisons or network analysis where the group in common is poorly matched
  - Superiority or non-inferiority is equivocal
- = Uncertain clinical benefit

# Uncertainty in economic evaluation

- Outcomes:
  - Extrapolation beyond the clinical trial
  - Convert surrogate outcome to health benefit
  - Probabilities of future events
- Utility weights:
  - Disease-specific health states can be represented by appropriate utility weight?
  - Instrument (if used) is sensitive for condition of interest
  - Jurisdiction-specific value set available (and used)?

# Uncertainty in econ evaluation

- Resource use and costs:
  - Adequately measured?
    - health state specific costs
  - Jurisdiction-specific costs can be applied to resources used?
- Modelling:
  - Appropriate model framework
    - Markov model? Decision analysis model, discrete event simulation?
  - Model developed to represent the progression of the condition?
    - Adapted for the jurisdiction of interest
  - Statistical analysis is appropriate
  - Validated output of the model!

## Types of (economic) uncertainty

Preferred term	Concept	Other terms used	Analogous concept in regression
Stochastic uncertainty	Random variability in outcomes between identical patients	<ul style="list-style-type: none"> <li>Variability;</li> <li>First-order uncertainty</li> </ul>	Error term
Parameter uncertainty	The uncertainty in estimation of the parameter of interest	<ul style="list-style-type: none"> <li>Second-order uncertainty</li> </ul>	Std error of estimate
Heterogeneity	The variability between patients that can be attributed to characteristics of those patients	<ul style="list-style-type: none"> <li>Variability;</li> <li>Observed or explained heterogeneity</li> </ul>	Beta coefficient
Structural uncertainty	The assumptions inherent in the model	<ul style="list-style-type: none"> <li>Model uncertainty</li> </ul>	The form of the regression model (e.g. linear, log-linear)

Source: Briggs et al. Model Parameter Estimation and Uncertainty: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-6. *Value in Health* 2012; 15, 835-42

## How is uncertainty dealt with?

- Simulations
- Deterministic Sensitivity Analysis
- Probability Sensitivity Analysis
- Collect more data?
- Collect higher quality data?
- Value of Information approaches?
  - EVPI
  - EVPPI
  - EVSI
  - Implementation-adjusted EVSI
- Other approaches???

# Issues for Discussion

This panel will:

- Introduce the problems with uncertainty
- Impacts on decision-making from uncertainty
- Practical ways of dealing with uncertainty

## Panelists

**Hansoo Kim**

*Bristol Myers Squibb, Australia*

- statistical uncertainty
- stochastic uncertainty and heterogeneity

**A/Prof Stephen Goodall, PhD**

*CHERE, University of Technology Sydney, Australia*

- structural uncertainty
- parameter uncertainty

**Prof Rosalie Viney, PhD**

*Chair of the Economics Sub-Committee, PBAC, Australia*

- uncertainty in the decision-making context of the PBAC

## Questions for Panelists

- Are there unified approaches for dealing with the different types of uncertainty in economic models?
- Are the current approaches used sufficient for decision-making?
- Is there one thing that all HTA bodies should be doing to address uncertainty (e.g. PSA)?
- Should HTA bodies fund research to collect additional data that may reduce uncertainty?