Bayesian Sensitivity Analysis of Economic Models

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Synopsis

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- Background
  - models, parameter uncertainty, sensitivity analysis
- Elicitation
  - specifying probability distributions for uncertain parameters, examples from MS model
- Sensitivity analysis
  - Bayesian methods, application to osteoporosis model
- Conclusions

Background

Models and parameters

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- Economic models are widely used in support of arguments of cost-effectiveness
- Invariably,
  - they have a number of parameters and assumptions that must be specified to run the model
  - the true values of these model inputs are not known
- Parameter estimates are typically drawn from a variety of sources

Sensitivity analysis

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- Uncertainty and inaccuracy in parameter estimates should be acknowledged
- To run the model with the estimated values and to pretend that the outputs from the model are precise assessments of cost-effectiveness is naïve and potentially misleading
- Sensitivity analysis explores the implications of uncertainty in model inputs

Varieties of SA

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- One-way SA
  - Vary one parameter at a time over range
- Multivariate SA
  - Vary parameters jointly
  - Factorial designs, Analysis of Variance
- Probabilistic SA
  - Assign probability distributions to parameters
  - Deduce distributions for outputs

Why use PSA?

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- More realistic representation of parameter uncertainty
- Comprehensive analysis of output uncertainty
  - Mean or median output is a better central estimate than the output from central estimates of inputs
  - Analysis of contributions from individual inputs
  - Chances of extreme outputs
- Recommended by NICE in their advice to sponsors

Why Bayesian methods?

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- Placing probability distributions on parameters is essentially Bayesian
  - Bayesian statisticians can offer considerable relevant expertise
- Propagating input uncertainty in PSA can be expensive in computer time
  - Modern Bayesian tools offer huge efficiency gains
  - They can also provide more informative analysis

Elicitation

Assessing uncertainty

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- Probability distributions on input parameters should represent uncertainty accurately
  - All sources of uncertainty should be recognised
  - Possible biases should be recognised
  - Should reflect consensus opinion
    - Varieties of opinion may be covered by scenarios
  - Should synthesise available information
- This is not easy!

The MS model

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- An economic model was built to assess beta-interferon and glatiramer acetate in treatment of multiple sclerosis
- Key inputs included
  - Natural history hazard rates for progression from each (E)DSS to the next
  - Treatment effects in reducing progression hazards

Natural history progression

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- Sources of uncertainty/error
  - Data from Canadian natural history dataset
    - Possible bias relative to UK
  - Parameters derived: mean sojourn times
    - Annual DSS data, so large rounding errors
  - Converted to hazards assuming exponential
    - Assumption
- Uncertainties modelled in terms of systematic and random components

Treatment effects

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- Effects of treatment in reducing progression from published sources
  - Sampling errors
  - Possible biases, presenting most favourable analysis
  - Clinical trial baselines and recruitment different
  - Different endpoints, do not relate directly to progression hazards
  - Relative risk assumed constant over (E)DSS
- Non-sampling uncertainty very substantial

Bayesian PSA

Monte Carlo PSA

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- Monte Carlo is the standard approach
  - Many random input configurations sampled from their probability distributions
  - Model run for each configuration => sample from output distribution
- Requires thousands of model runs
- Provides overall assessment of output uncertainty
  - Thousands more runs needed for deeper analysis

Other methods

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- There is a substantial literature on sensitivity analysis of complex computer models
- This has not yet filtered into health economics
- Analysis is often focussed on understanding the model and identifying influential inputs
- Recently developed Bayesian methods offer enormous reduction in the number of model runs needed

Osteoporosis model

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- Uncertainty over relative risks of fractures
- Available clinical data only allow these to be estimated with a substantial margin of error
- The model is very computer-intensive
  - Patient-level simulation model
  - A single run, with specified values for the relative risks, takes 1.5 hours
  - MC methods would be completely impractical

Model runs

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- 4 uncertain inputs
  - Relative risks of fractures to the hip, spine, humerus and forearm
- 41 runs of the model
  - Needed to cover RR values appropriate for several alternative drugs
  - Only about 20 runs informative for a given drug
  - Unlike MC, parameter configurations not random, but *chosen* to make maximal use of these few runs

CEAC

The Cost-Effectiveness Acceptability Curve gives the probability, based on available evidence, that this drug is more cost-effective than standard, as a function of the willingness to pay K (pounds per QALY)

Partitioning the variance

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- Variance of incremental net benefit is partitioned according to contributions from each uncertain parameter
- Uncertainty in the RR of hip fracture is most influential (39%), then spinal fracture (14%)
- Interactions are very important (31%)

Main effects

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- The graphs show the effect of varying each parameter, when *averaged* over the uncertainty in other parameters
- We can see that RR for hip fractures is most influential, but can also see the nature of its influence

Joint effects

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- This shows the joint effect of the RRs for hip and spinal fractures, averaged over other parameters
- The importance of interactions is evident

Conclusions

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- Probabilistic Sensitivity Analysis is an important process in the use of economic models
- The specification of probability distributions for parameters is crucial and difficult to do well
  - Bayesian expertise in elicitation can help
- The technology of implementing PSA is complex, and MC methods will often be inappropriate
  - New Bayesian tools offer efficiency savings and access to more informative analyses