UNIVERSITY of York
RESEARCH

CHE
Centre For Health Economics

Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 7: Uncertainty, heterogeneity and VOI
7.2: Probabilistic sensitivity analysis

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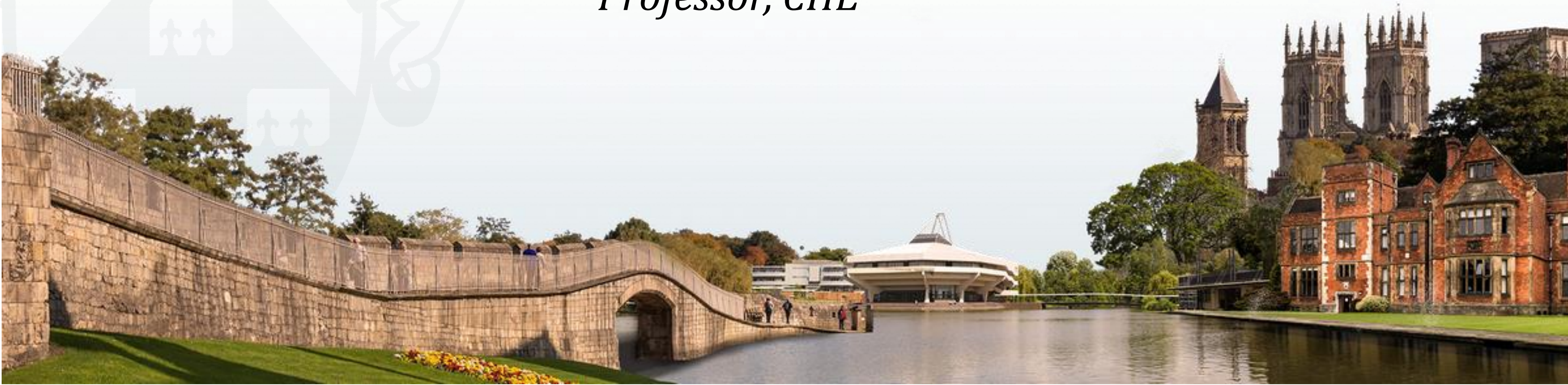
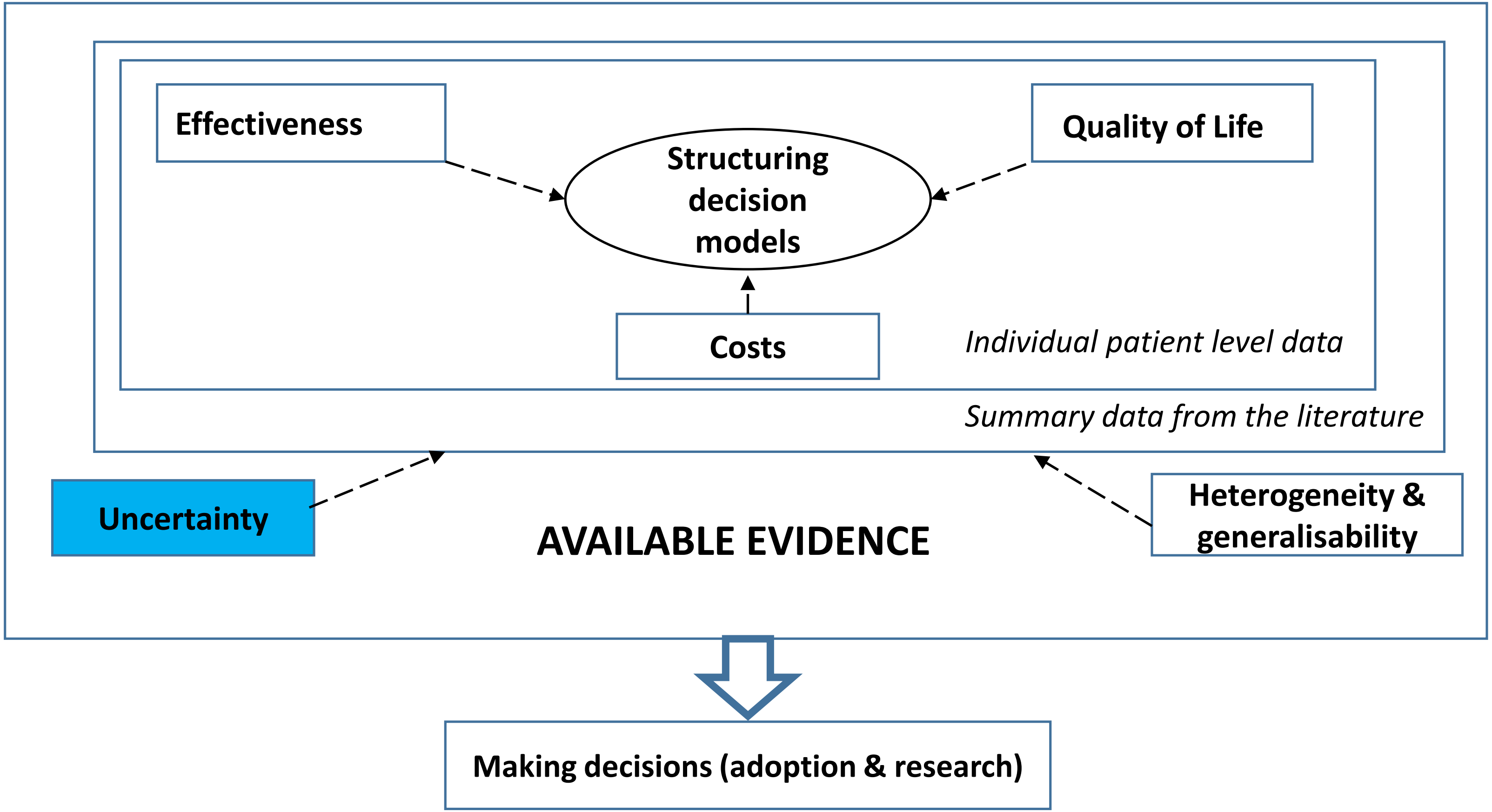


Course structure – where are we up to?



Objectives

- Understand what probabilistic sensitivity analysis is, and the uncertainty it encompasses
- Understand how to implement probabilistic sensitivity analysis in a decision model
- Understand how to compute cost-effectiveness results after undertaking a probabilistic sensitivity analysis

Beyond deterministic sensitivity analysis

- '5.8.11 The use of univariate and best- or worst-case sensitivity analysis is an important way of identifying parameters that may have a substantial impact on the cost-effectiveness results and of explaining the key drivers of the model. However, such analyses become increasingly unhelpful in representing the combined effects of multiple sources of uncertainty as the number of parameters increase. The use **of probabilistic sensitivity analysis** can allow a more **comprehensive characterisation** of the parameter **uncertainty associated with all input parameters**.'

NICE Guide to the methods of technology appraisal 2013

Probabilistic sensitivity analysis (PSA): Stages

- Assigning distributions to represent uncertainty
  - Estimates of probabilities, quality of life weights and costs are replaced with specified probability distributions
- Propagating uncertainty
  - Randomly select value from each distribution
  - Model evaluated many times (>1,000)
  - Distribution of and average of simulated model results used in decision making
- Reporting results
  - Distribution of outcomes for each strategy
  - Probability that a particular intervention is optimal

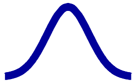
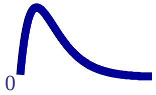
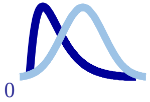
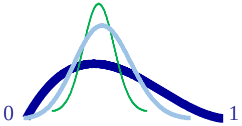
Assigning distributions

- Primary data (individual patient level)
  - Fit regression models and use the resulting variance covariance matrices
  - Empiric distribution from bootstrap samples
- Secondary data (aggregate level)
  - Assign distribution using information reported in the literature
  - This is the usual situation we find ourselves in and is covered in what follows
- No primary or historical evidence
  - Assign distribution using information elicited from experts
  - Elicitation methods available

Choosing a distribution for a parameter

- Match what is known about the model input with the characteristics of the distribution
  - Common distributions include the Normal, Log-normal, Gamma and Beta
- Alternative distributions defined by
  - Logical constraints on the parameter
    - Can it take values less than zero?
  - Type of data
    - Discrete like number of admissions or continuous like weight?
  - Method of parameter estimation or data generation
    - Informed by the output from an ordinary least squares regression analysis

Commonly used distributions

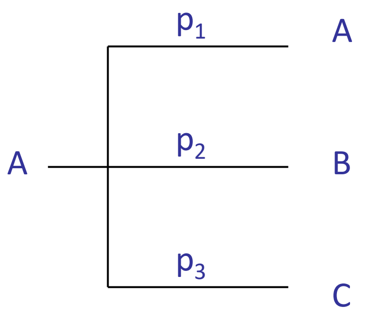
Distribution	Specified with	Characteristics	Drawing values in Excel
Normal 	- Mean, μ - Standard deviation (SD) of mean, σ	- Values unbounded - Continuous; symmetrical - Mean, median, mode at line of symmetry - 95% of values within 2 SD of mean	NORM.INV(RAND(), mean, sd)
LogNormal 	- On log scale - Mean, μ - Standard deviation (SD) of mean, σ	- Any positive value > 0 - Continuous; right (positively) skewed	LOGNORM.INV(RAND(), mean, sd)
Gamma 	- Shape, α - Scale, β	- Any positive value ≥ 0 - Continuous; symmetrical or right skewed - Method of moments: $\mu=\alpha\beta$ and $\sigma^2=\alpha\beta^2$	GAMMA.INV(RAND(), alpha, beta)
Beta 	- α (# of successes) - β (# of failures)	- Any positive value ≥ 0; bounded 0-1 - Flexibly shaped - $\alpha+\beta=n$ (sample size) - Method of moments: $\mu=\alpha/(\alpha+\beta)$ and $\sigma^2=\alpha\beta/[(\alpha+\beta)^2(\alpha+\beta+1)]$	BETA.INV(RAND(), alpha, beta)

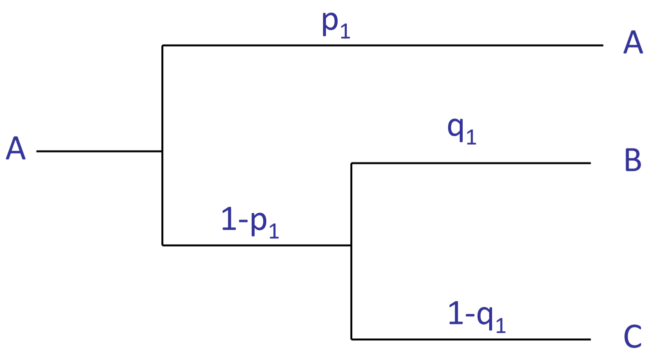
Matching distributions to input characteristics

Parameter	Distribution	Values
Transition probabilities	Beta	Alpha, Beta
Relative treatment effect	Lognormal	Mean, SD
Costs	Gamma	Shape, Scale
Dis-utilities	Gamma	Shape, Scale

Other issues

- Variables enter only once
- Multiple events





Note: $q_1 = p_2 / (1-p_1)$

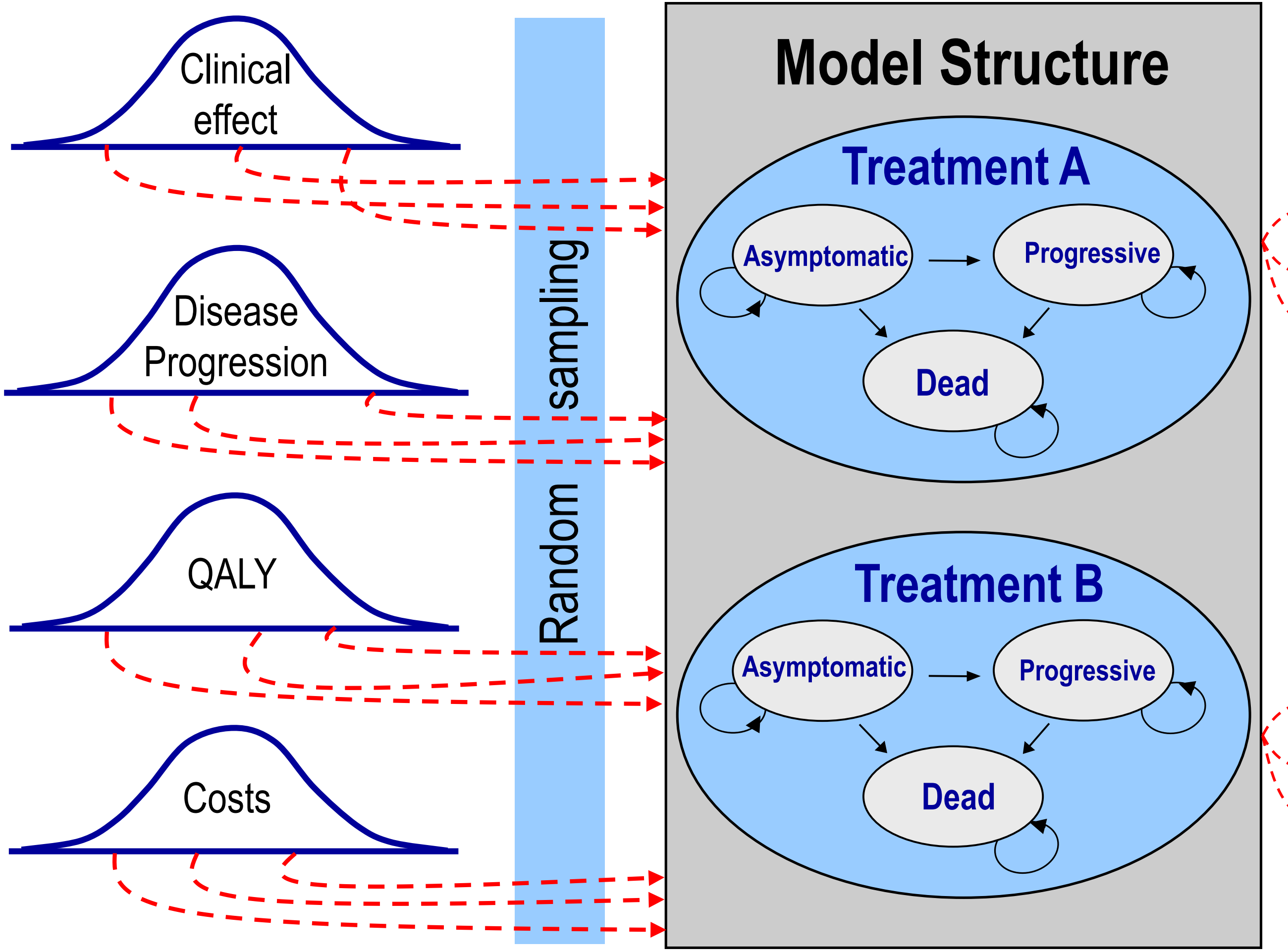
  - Restructure the tree (conditioned into dichotomous transitions)
  - Dirichlet distribution

- Characterise correlation between parameters where possible

Propagating uncertainty

- Monte Carlo simulation – 2nd order uncertainty
  - Randomly draw a set of input values (one for each parameter)
  - Put a cohort through the model
  - Determine the expected outcomes – cost, effect, etc
  - Repeat a large number of times (> 1,000)
  - Distribution of expected outcomes
- In non-linear decision models, probabilistic methods provide the best estimates of mean costs and outcomes
  - Mean of the distribution of expected outcomes ≠ outcome with inputs set to mean values

Propagating uncertainty



Treatment A	
QALY	Cost
1	£10,000
0	£ 5,000
2	£15,000
1	**£10,000**

Treatment B	
QALY	Cost
2	£30,000
3	£20,000
4	£40,000
3	**£30,000**

Should the intervention be adopted?

Treatment A	
QALY	Cost
1	£10,000
0	£ 5,000
2	£15,000
1	**£10,000**

Treatment B	
QALY	Cost
2	£30,000
3	£20,000
4	£40,000
3	**£30,000**

$$\text{ICER} = \frac{\text{Additional cost}}{\text{QALYs gained}} = \frac{£20{,}000}{2\ \text{QALYs}} = £10{,}000 \text{ per QALY}$$

Calculate ratio of means, NOT mean ratio

- **Is the ICER less than the cost-effectiveness threshold?**
- **Is the health gained more than the health that would have been produced if the resources had been spent otherwise?**

£10,000 per QALY < £20,000 per QALY → Treatment B is cost-effective

- **Is the net health benefit (NHB) positive?**

NHB= QALYs gained – (additional costs/threshold)

= 2 – (£20,000/£20,000)

= 1 QALY > 0 → Treatment B is cost-effective

Summary

- You should now understand the process of undertaking probabilistic sensitivity analysis
- You should understand how to match distributions to parameter characteristics
- You should understand the process of Monte Carlo simulation

- In Part 7.3 we will learn about presenting and interpreting the results of probabilistic sensitivity analysis