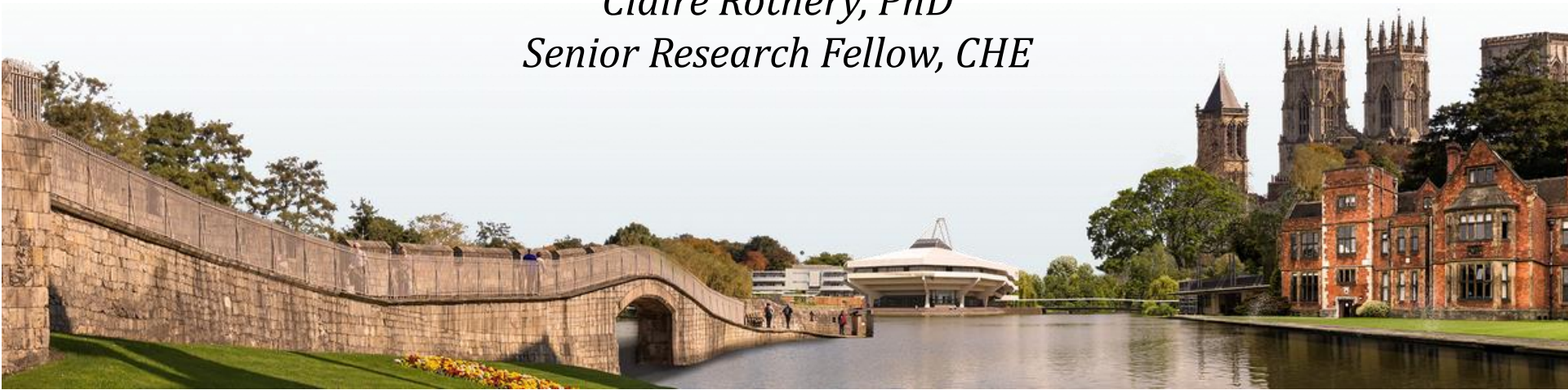
Online Advanced Methods for Cost-Effectiveness Analysis

Lecture 7: Uncertainty, heterogeneity and VOI
7.5: Informing research decisions

Claire Rothery, PhD
Senior Research Fellow, CHE



Objectives

- Estimate the expected value of sample information (EVSI) and the expected net benefit of sample information (ENBS)
- Interpret EVSI and ENBS for informing research design
- Implications of VOI for policy decisions
    - coverage with evidence development
    - identifying research priorities
    - link between approval, price and research decisions

Setting research priorities

- EVPI and EVPPI
  - Maximum return to research
  - Comparing the EVPI to the opportunity costs of research
  - Comparing EVPI across technologies
  - Comparing EVPPI to focus research design

- EVSI and ENBS
  - Identify technically efficient research designs
  - Allocations between clinical areas
  - Allocation between research and service provision

What type of research design?
Expected value of sample information (EVSI)

- In practice unlikely to obtain perfect information
  - Additional research will reduce, rather than eliminate uncertainty
- Research design may include sample size, allocation of patients between arms of clinical trial, length of follow-up, endpoints to include
- EVSI provides the value of a decision based on having additional sample information. It predicts possible sample results that would be obtained from a study with a sample size of n
- To establish if the study is an efficient use of resources, the societal value of the study is compared to the costs of gathering the sample information
- Sufficient condition for further research
  - Expected net benefit of sampling (ENBS) = EVSI - cost of research
  - If ENBS > 0 for a particular sample design then further research is worthwhile

Expected value of sample information (EVSI)

Steps required to calculate EVSI as function of study design and sample size:

1. Sample from the prior distributions

   e.g. $\theta \sim \text{Beta}(\alpha = 3.64, \beta = 47.14)$

2. Then sample likelihood to generate possible sample results for size n, $D|\theta$

   e.g. $D \sim \text{Binomial}(\theta, n)$

3. Combine the prior and predicted sample distributions to form predicted posterior results for each sample

   e.g. $X' \sim \text{Beta}((\alpha+n\theta), (\beta+n-n\theta))$

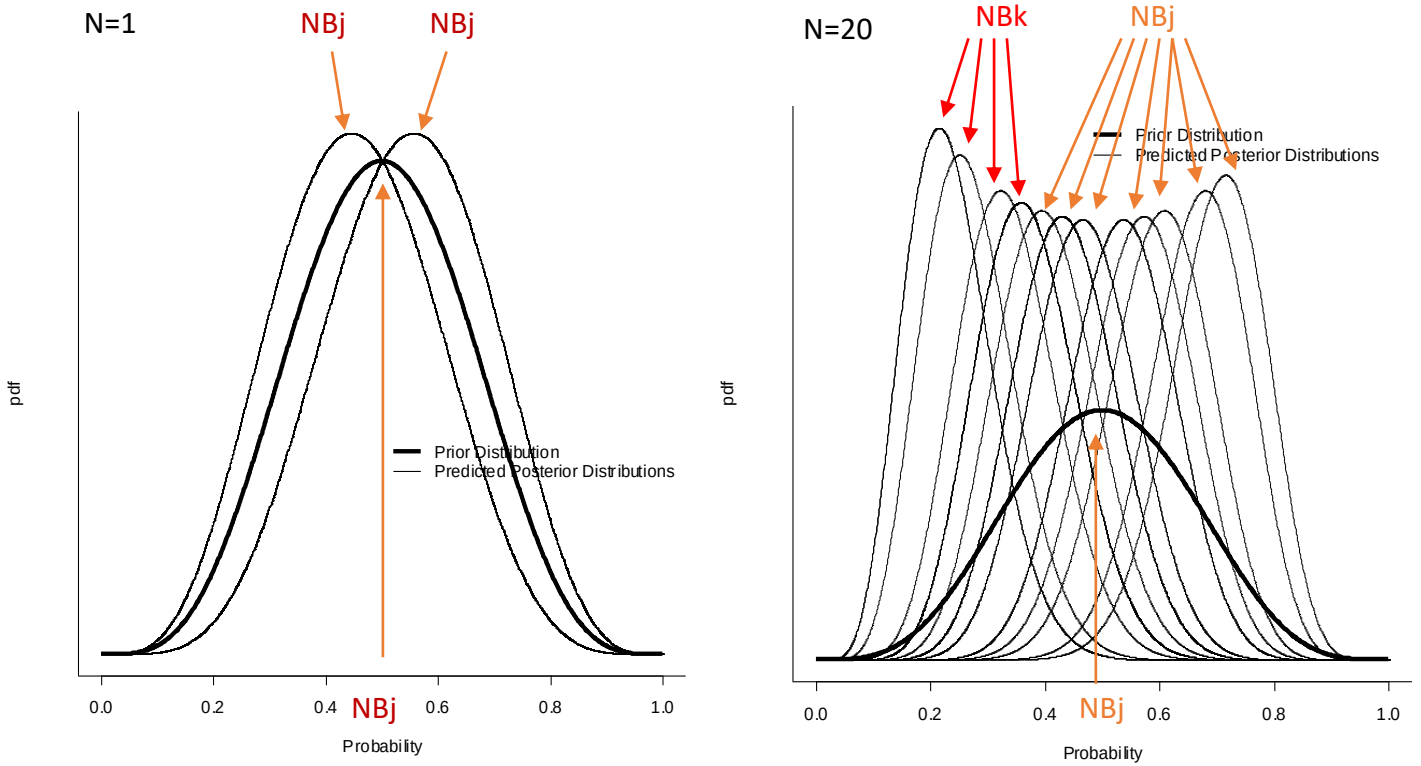
4. Calculate NB for each predicted posterior and choose the treatment with the highest NB

5. Since the actual results of each sample are not known in advance, average the maximum expected NB over the distribution of possible sample results: $E_\theta E_{D|\theta} \max_j E_{\theta|D} NB(j, \theta)$

   EVSI = NB with sample information – NB with current information

   $$EVSI = E_\theta E_{D|\theta} \max_j E_{\theta|D} NB(j, \theta) - \max_j E_\theta NB(j, \theta)$$

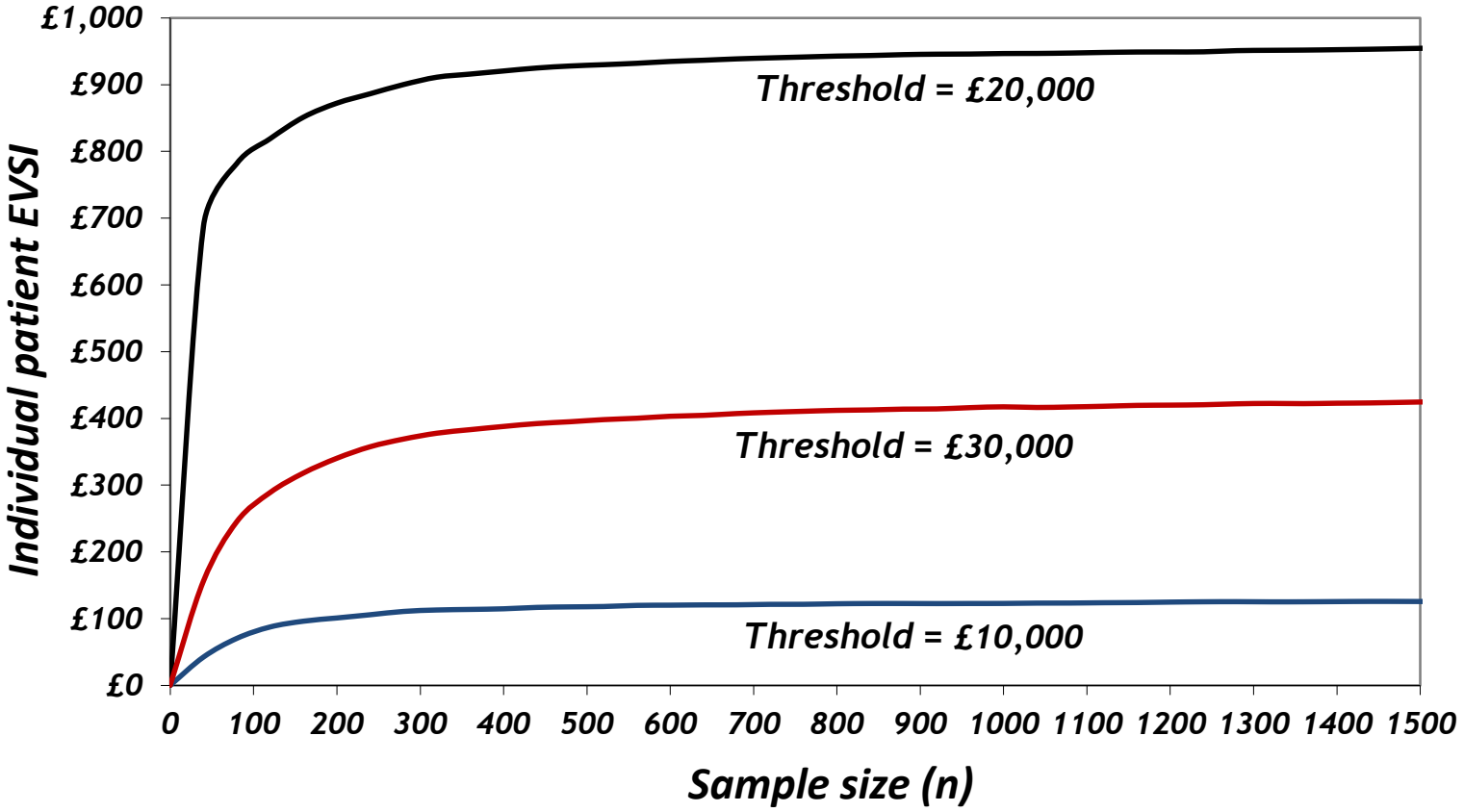
Expected value of sample information (EVSI)



Source: Karl Claxton, Centre for Health Economics, York

Ref: Ades AE, Lu G, Claxton K. Expected Value of Sample Information Calculations in Medical Decision Modeling. *Medical Decision Making* 2004; 24(2): 207-227

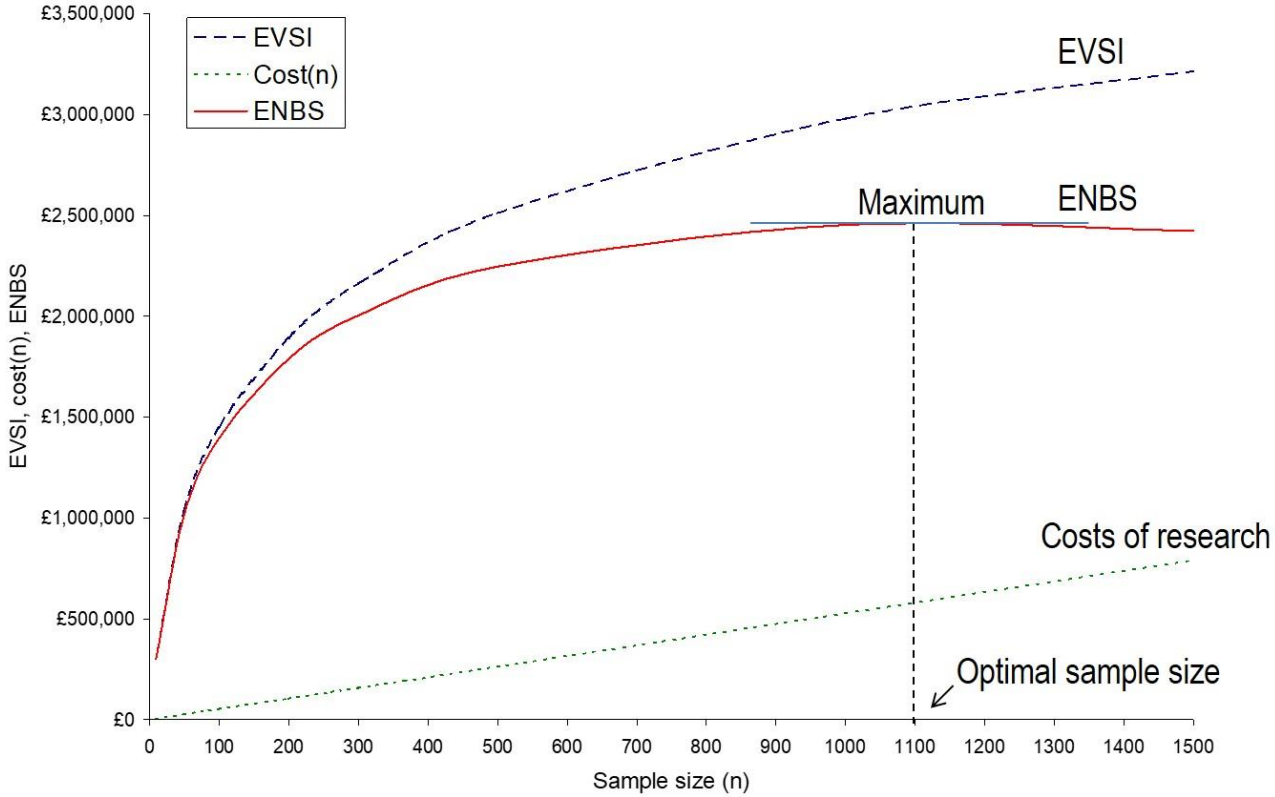
EVSI for different sample sizes



Is research an efficient use of resources?

- ENBS = Population EVSI - cost of research
- Cost of research as function of study design and sample size
  - Costs of running study and opportunity costs to patients
  - Patients enrolled in study no longer part of population to benefit from additional information (acute condition)
- Use ENBS to prioritise research and in place of traditional power calculations
  - ENBS > 0 for a particular sample design then further research is worthwhile
  - Choose between alternative research designs, e.g. appropriate length of follow-up, sample size, where the **ENBS reaches a maximum**

Expected net benefit of sample information (ENBS)



Feasibility of research

- Likelihood of research
  - Research itself may be uncertain prospect (fail to complete)
- Type of research design
  - Observational versus experimental
- If treatment is adopted and available outside research
  - Randomisation may be viewed as unethical
  - Patients may be unwilling to randomise (or drop out)
  - Manufacturer lacks incentive to fund research
- Time to research versus time horizon for decision
  - Value of research only realised from time research reports

Opportunity costs of adoption

- Decision to adopt/reject a technology based on expected net benefit
  - No impact of adoption decisions on research
- Sunk costs with implementation of technology, i.e. a cost that has already been incurred and cannot be recovered
  - Delay adoption until research reports?
  - Opportunity costs of delay
- Adoption reduces further research
  - Incentives/ethics, e.g. may be considered unethical to enrol patients into research if the technology is available for widespread use
  - Unable to enforce conditional permissions/coverage with evidence

When to approve the technology?

Approve: Could impact the prospects of acquiring further evidence

Reject: Could restrict patient access to promising new technologies

Additional policies overcome the problems associated with making coverage decisions under uncertainty:

Only in research (OIR): 'No' decision until further evidence establishes value

Approve with research (AWR): 'Yes' decision until further research is completed and guidance is established

What assessments are needed?

- Expected cost-effectiveness
- Irrecoverable costs
  - Costs committed by approval that cannot be recovered
    - Capital costs of long lived equipment (training and learning)
    - Initial losses (negative NB) offset by later gains
    - Significance depends on whether initiation of treatment can be delayed
- Value of additional evidence
- The need for evidence, type of evidence, design of research
- Uncertainty that cannot be resolved by research but only over time
- Are the benefits of early approval greater than the opportunity costs?

Framework for health technologies

Claxton K, *et al*. (2012) Informing a decision framework for when NICE should recommend the use of health technologies only in the context of an appropriately designed programme of evidence development. *Health Technology Assessment*; vol. 16

Summary

- Policy analysis based on value of information analysis can be used to consider the value of
  i. research compared to its expected costs;
  ii. being able to conduct research while a technology is approved;
  iii. the trade-off between the expected benefits to current patients from early access and the benefits to future patients from more research
- Understanding the relationship between the time taken for research to report and the value of the evidence can help inform
  i. investments which might make research findings available quickly;
  ii. the trade-off implicit in the choice of alternative research designs;
  iii. those areas where research must be reported quickly to be of value

Reading list for lecture 7 (parts 7.1 – 7.3)

- Briggs AH. Handling uncertainty in cost-effectiveness models. *PharmacoEconomics* 2000; 17(5): 479-500.
- Briggs AH, Goeree R, Blackhouse G, O'Brien BJ. Probabilistic analysis of cost-effectiveness models: choosing between treatment strategies for gastroesophageal reflux disease. *Medical Decision Making* 2002; 22: 290-308.
- Briggs A, Claxton K, Sculpher MJ. *Decision modelling for health economic evaluation*. Oxford University Press, 2006.
- Claxton K. Characterising, reporting, and interpreting uncertainty. In: Drummond, Sculpher, Claxton, Stoddart and Torrance *eds. Methods for the Economic Evaluation of Health Care Programmes.* Oxford, UK. Oxford University Press, 2015.
- Fenwick E, O'Brien B, Briggs AH. Cost-effectiveness acceptability curves – facts, fallacies and frequently asked questions. *Health Economics* 2004; 13: 405-415.
- van der Bles AM, van der Linden S, Freeman ALJ, et al. Communicating uncertainty about facts, numbers and science. Royal Society Open Science 2019;6: 181870

Reading list for lecture 7 (parts 7.4 – 7.5)

- Fenwick E, Stotten L, Knies S, et al. Value of information analysis for research decisions: an introduction report 1 of the ISPOR Value of Information Analysis Task Force. Value in Health. 2020;23(2):139–150.
- Rothery C, Strong M, Koffiberg H, et al. Value of information analytical methods emerging good practices: report 2 of the ISPOR VOI Task Force. Value in Health. 2020;23(3):277–286.
- Claxton K and Sculpher MJ. Using value of information analysis to prioritise Health research: some lessons from recent UK experience. *PharmacoEconomics* 2006, 24:1055-1068.
- Claxton K, Palmer S, Longworth L, et al. Informing a decision framework for when NICE should recommend the use of health technologies only in the context of an appropriately designed programme of evidence development. Health Technology Assessment 2012;16.
- Claxton K, Griffin S, Koffijberg H and McKenna C. How to estimate the health benefits of additional research and changing clinical practice. *BMJ* 2015; 351.