Online Advanced Methods for Cost-Effectiveness Analysis

Lecture 7: Uncertainty, heterogeneity and VOI
7.4: Introduction to Value of Information (VOI)

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Objectives

- Understand why uncertainty matters for making adoption and research decisions
- Introduce the concept of the value of additional evidence
- Estimate the expected value of perfect information (EVPI) and the expected value of perfect parameter information (EVPPI)
- Interpret EVPI and EVPPI for research decisions

How uncertain is a decision?

Realisations that could occur in clinical practice	Net health effects (e.g. QALYs)			Best outcome for each realisation
	Treatment A	Treatment B	Best treatment choice	
Realisation 1	9	12	B	12
Realisation 2	12	10	A	12
Realisation 3	14	17	B	17
Realisation 4	11	10	A	11
Realisation 5	14	16	B	16
Expected (mean)	**12**	**13**		**13.6**

What's the best we can do now?

Choose B and expect 13 QALYs

But we are not always right:

Chance that B is the best = 3/5 = 0.6

Chance that A is the best = 2/5 = 0.4

If we adopt B the probability of error = 0.4

Why uncertainty matters?

- Uncertainty refers to the fact that we cannot know with absolute certainty what the expected (mean) effects of the intervention are
- There will always be a chance that the ‘wrong’ adoption decision is made resulting in a loss of health benefit and resources
- Basing decisions about a health care intervention on expected health effects does not address the question about whether the current evidence is a sufficient basis for guiding decisions in clinical practice. It fails to address the question of whether further research is needed before making a decision that could potentially harm patients due to the consequences of the uncertainty
- The value of uncertainty is the value of future evidence to eliminate that uncertainty

Adoption and research decisions

A number of conceptually distinct but simultaneous decisions to be made:

- Which technology should be adopted into clinical practice given the existing evidence base and the uncertainty surrounding outcomes and resource use?
- Is additional evidence required to support the use of the technology?
  - How uncertain are the expected benefits?
  - Does this uncertainty matter (will it change the adoption decision)?
  - How much does it matter (consequences of getting it wrong)?
- What type of evidence would be most valuable?
- Which research designs would be worthwhile?
- When to approve the technology?
  - Early approval? Can the evidence be provided with approval?

Is further evidence required?

- Information is valuable because it reduces the expected consequences of the uncertainty

  - Better decisions from more information → greater health gains

- Identify the consequences that can result from uncertainty and the likelihood of these consequences occurring

  - VOI aggregates the probability-weighted consequences to yield a net health impact of uncertainty for each alternative intervention

- Compare the value of research to cost of obtaining additional evidence
  - Expected value of research > cost of research → additional evidence is valuable
  - Expected value of research < cost of research → current evidence may be sufficient

Expected value of perfect information (EVPI) per individual

- With current information, must choose: $\max_j E_\theta \, NB(j, \theta)$
  where j are the alternative interventions and
  θ are the uncertain parameters
- If the uncertainty could be resolved (perfect information), the decision maker would choose to maximise the net benefits for each realisation of uncertainty: $\max_j NB(j, \theta)$
- True realisations are unknown, so we must average over all possible values: $E_\theta \max_j NB(j, \theta)$
- Additional value of information, EVPI = NB (perfect) – NB (current)

$$EVPI = E_\theta \max_j NB(j, \theta) - \max_j E_\theta \, NB(j, \theta)$$

Calculating the EVPI – an example

Realisations of uncertainty that could occur in clinical practice	Net health effects (QALYs)			Best outcome for each realisation, max NB(j,θ)
	Treatment A j = 0	Treatment B j = 1	Best treatment choice	
θ_1	9	12	B	12
θ_2	12	10	A	12
θ_3	14	17	B	17
θ_4	11	10	A	11
θ_5	14	16	B	16
E_θ NB(j,θ)	12	13		13.6

What's the best we can do now?

Choose B, expect 13 QALYs, gain 1 QALY

Could we do better?

With perfect information, expect 13.6 QALYs

$$EVPI = E_\theta \max_j NB(j, \theta) - \max_j E_\theta NB(j, \theta)$$

$$= 13.6 - 13 = 0.6 \text{ QALYs per patient}$$

EVPI at a population level

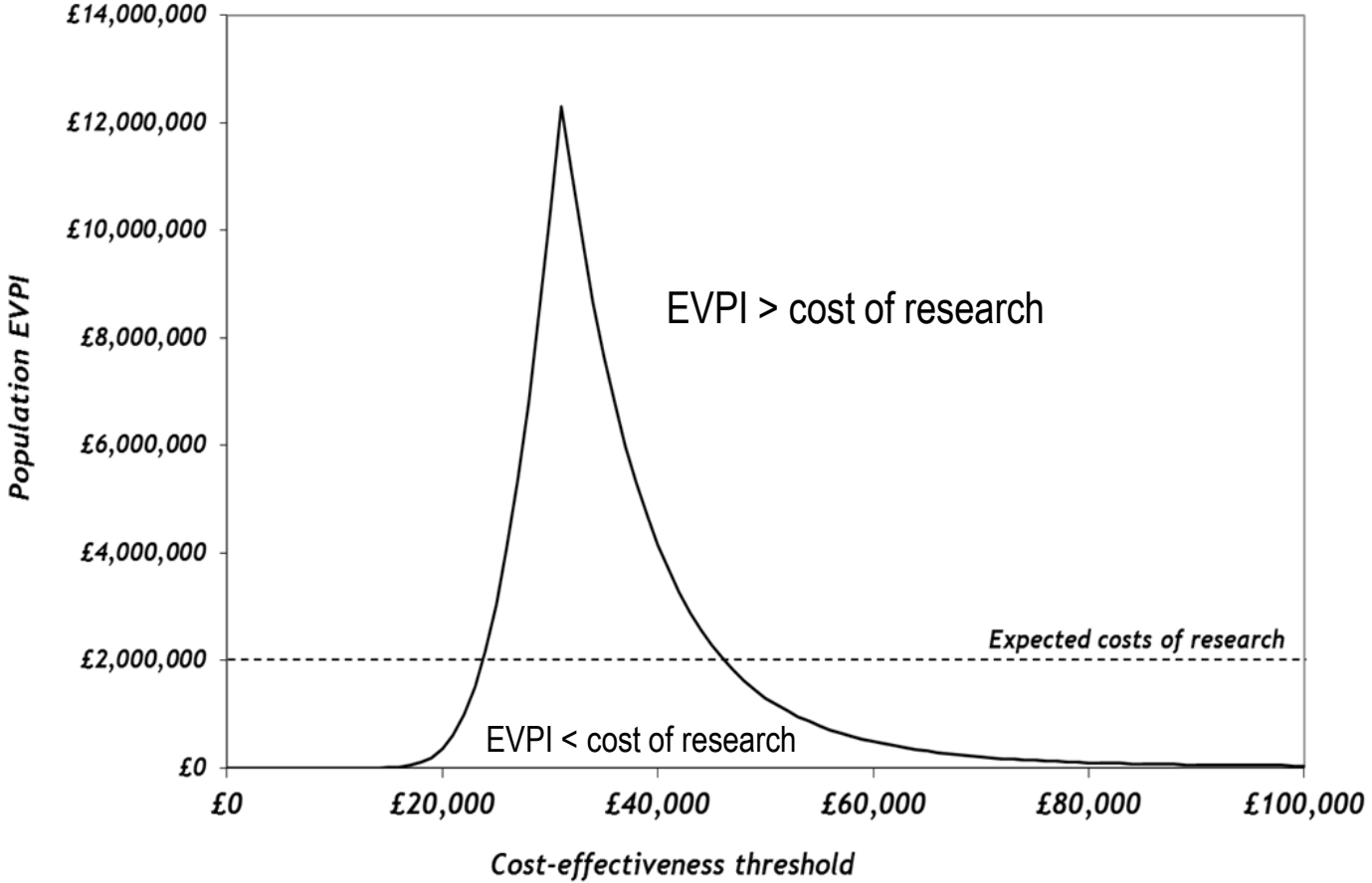
- EVPI at a population level
  - Multiply the 'per patient EVPI' by the number of times this information is used to inform treatment choice (size of the beneficiary population)
  - Depends on size of prevalent and incident population, P_t, I_t
  - Depends on time horizon over which information is valuable, T

$$Population\ EVPI = EVPI. \sum_{t=1}^{T} \frac{I_t}{(1+d)^t}$$

d, discount rate

- Provides an expected upper bound on the value of research
  - Population EVPI > cost of research
  - If EVPI is lower than the expected costs of conducting further research then it is not cost-effective to conduct further research, i.e. EVPI provides a necessary condition for conducting research

EVPI at a population level



Relationship between EVPI, ICER and threshold

- As ICER approaches cost-effectiveness threshold
  - Net benefit of alternatives more similar (INB close to 0)
  - Likelihood of error increases
  - Consequences of error decrease
- For a cost-effective technology (ICER < threshold)
  - Reducing price will reduce EVPI
  - Reducing current uncertainty will reduce EVPI
- EVPI can be used as a first hurdle to identify research which is potentially cost-effective
  - Identify research priorities by comparing the net value of research (EVPI minus costs of research) across technologies

What type of evidence is required?

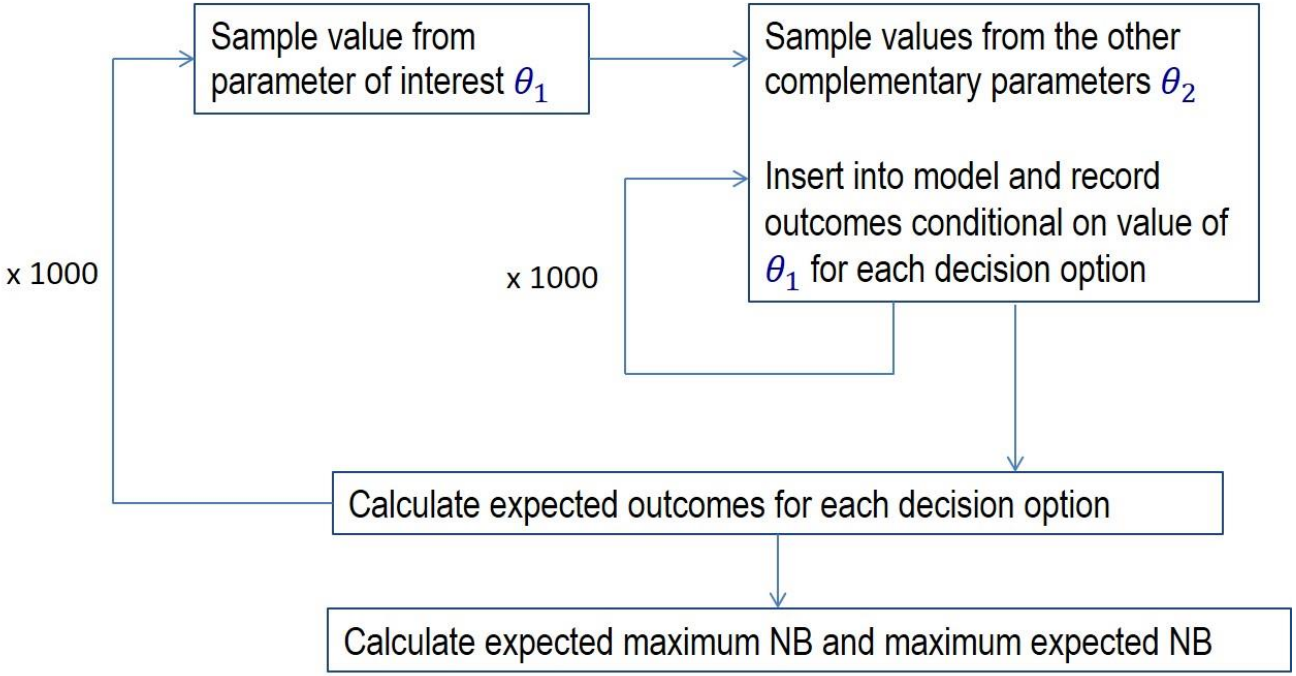
Expected value of perfect information for parameters (EVPPI)

- EVPPI considers the value of particular elements of the decision problem in order to direct and focus research towards those areas where the elimination of uncertainty has the most value
- The consequences of uncertainty over each of the model parameters can be evaluated: $\theta = \{\theta_1, \theta_2, \ldots.\}$
- Estimate cost of uncertainty that is attributable to:
  - Single parameters or groups of parameters e.g. costs, effectiveness
  - Shows sensitivity of model results to inputs and consequences of error
- For each parameter or group there will be a different potential value of research and appropriate research design

Calculating EVPPI

$$EVPPI_{\theta_1} = E_{\theta_1} \max_j E_{\theta_2|\theta_1} NB(j, \theta_1, \theta_2) - \max_j E_{\theta} NB(j, \theta)$$

θ
- θ_1 = parameter of interest
- θ_2 = other uncertainties (complementary parameters)

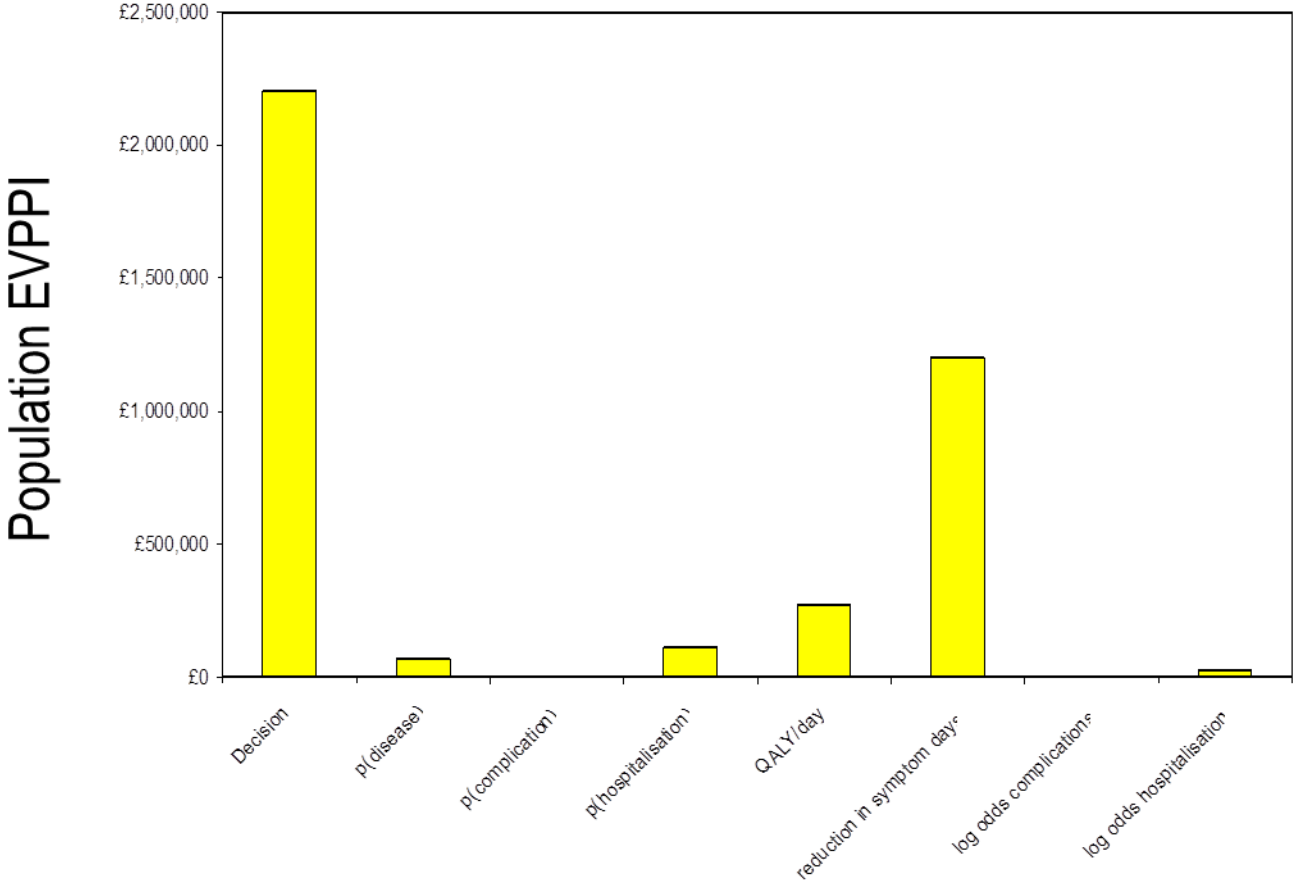


Issues in calculating EVPPI

- Two-level sampling algorithm (unless model is linear)
  - Sample parameter of interest (outer loop)
  - Analyse model probabilistically (inner loop)
- Analysis time
  - How many simulations? Which parameters/groups of parameters to include?
- Sum of EVPPI ≠ EVPI
- Knowing θ1 alters value of θ2
- Can calculate EVPPI as group to embed correlation between parameters
- More flexible regression-based methods available to reduce to single-loop sampling (efficient EVPPI computation)

Ref: ISPOR Task Force report. Value of Information Analytical Methods: Report 2 of the ISPOR Value of Information Analysis Emerging Good Practices Task Force. Rothery et al (2020)

EVPPI at a population level



Summary

- Principles of uncertainty and value of information
  - Why uncertainty matters
  - Scale of the consequences of uncertainty
  - Value of additional evidence

- 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

- In Part 7.5 we will learn about EVSI