11. Value of information

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STAT0019 - Bayesian Methods in Health Economics, UCL

Summary

- What is Value of Information and stupid examples?
- Summarising uncertainty and PSA
- Research priorities

References

Bayesian Methods in Health Economics, chapters 3.5.2, 3.5.3 Library | Book website (CRC) | Book website | Code

Evidence Synthesis for Decision Making in Healthcare, chapter 12 Library | Book website

Bayesian Cost-Effectiveness Analysis with the R package BCEA, chapter 4.3 Book website (Springer) | Book website

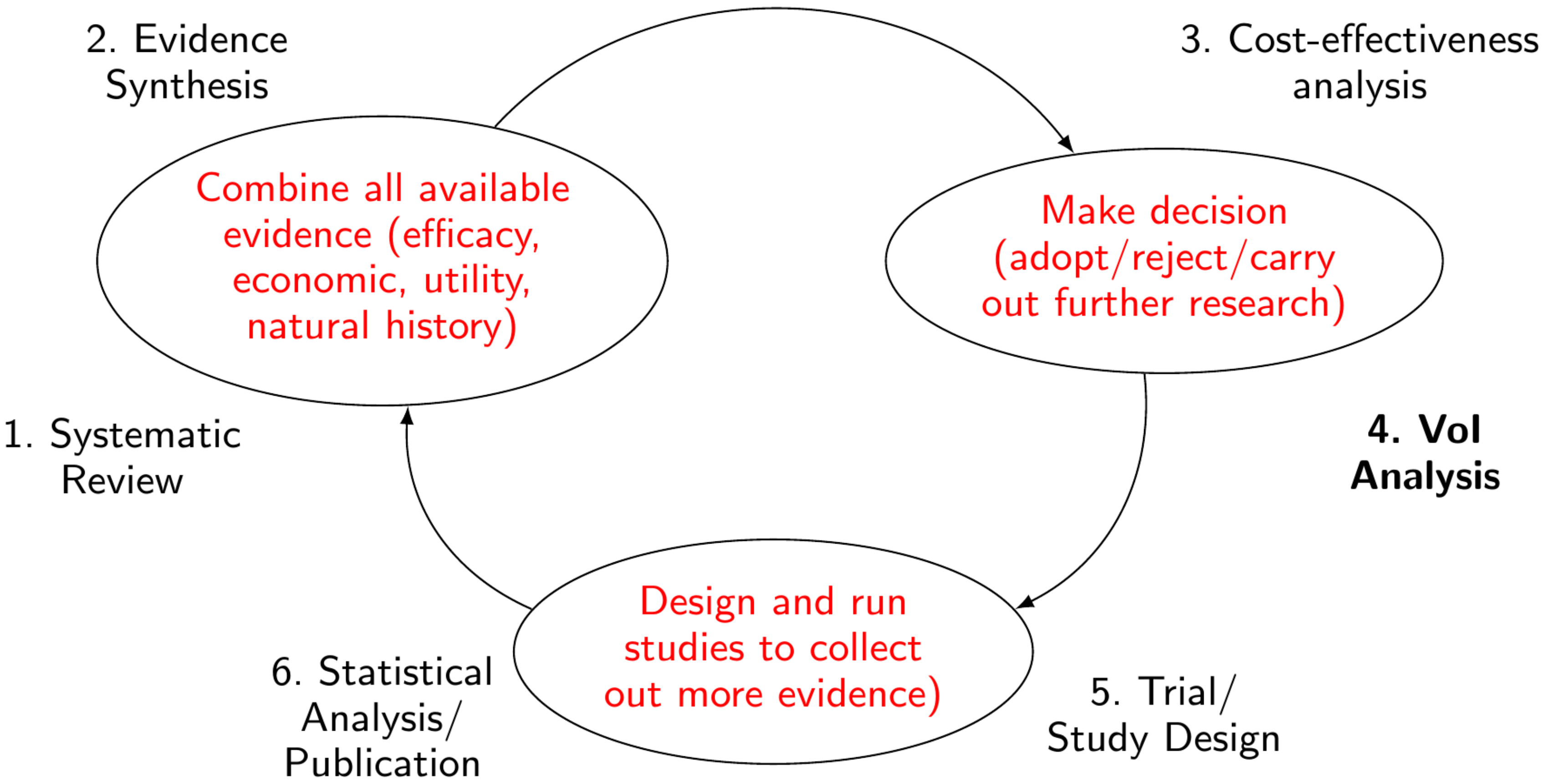
(A tale of two stupid examples)

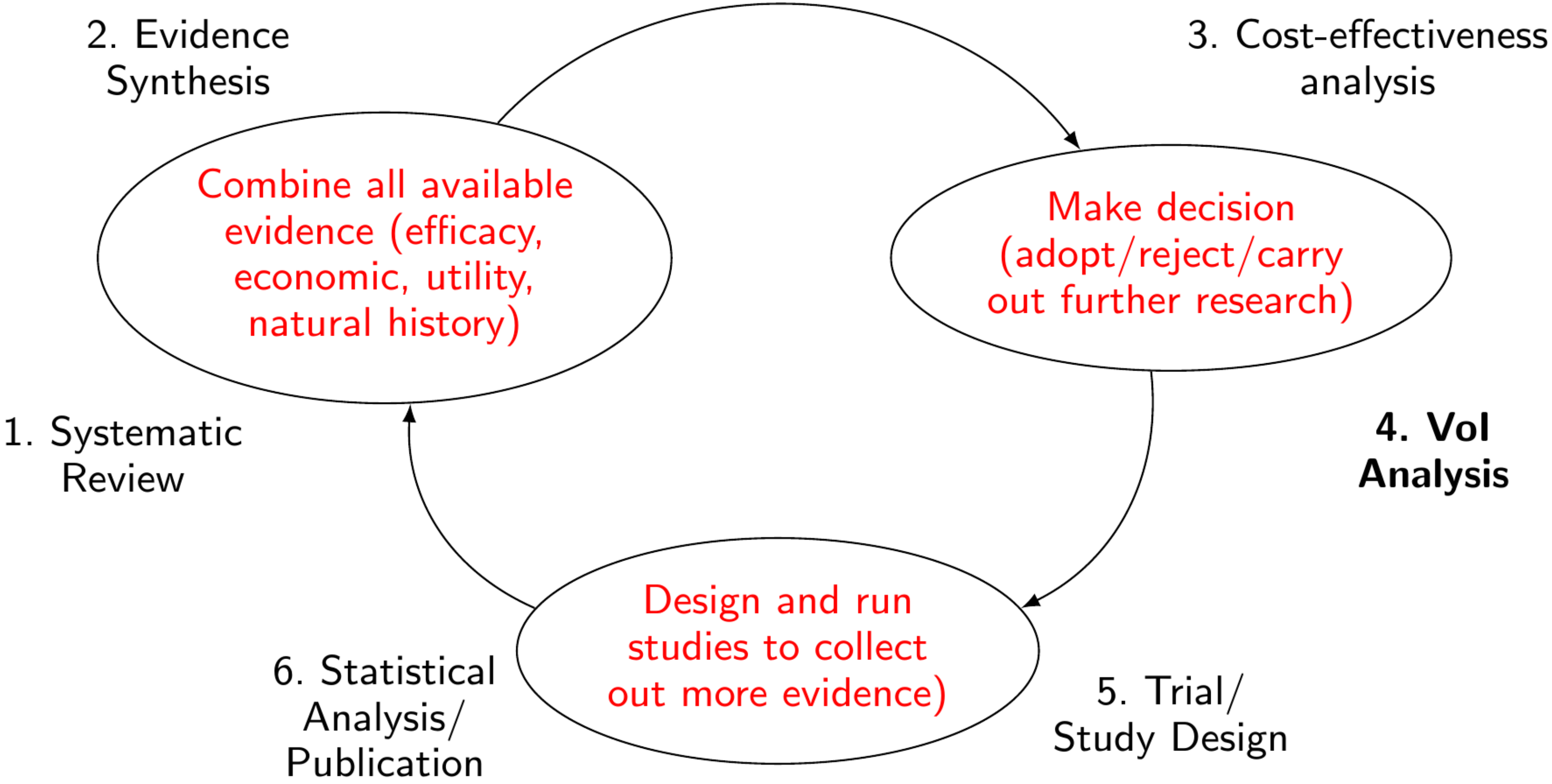
- **Example 1**: Intervention $t = 1$ is more cost-effective, given current evidence
  - Pr$(t = 1$ is cost-effective$) = 0.51$
  - If we get it wrong:
    - Increase in population average costs $=$ £3
    - Decrease in population average effectiveness $=$ 0.000001 QALYs
  - Large uncertainty/negligible consequences$\Rightarrow$**can afford uncertainty**!

(A tale of two stupid examples)

- **Example 1**: Intervention $t=1$ is more cost-effective, given current evidence
  - $\Pr(t=1 \text{ is cost-effective}) = 0.51$
  - If we get it wrong:
    - Increase in population average costs $=$ £3
    - Decrease in population average effectiveness $=$ 0.000001 QALYs
  - Large uncertainty/negligible consequences$\Rightarrow$**can afford uncertainty**!

- **Example 2**: Intervention $t=1$ is more cost-effective, given current evidence
  - $\Pr(t=1 \text{ is cost-effective}) = 0.999$
  - If we get it wrong:
    - Increase in population average costs $=$ £1000000000
    - Decrease in population average effectiveness $=$ 999999 QALYs
  - Tiny uncertainty/dire consequences$\Rightarrow$**probably should think about it...!**


2. Evidence Synthesis
3. Cost-effectiveness analysis
Combine all available evidence (efficacy, economic, utility, natural history)
Make decision (adopt/reject/carry out further research)
1. Systematic Review
4. VoI Analysis
Design and run studies to collect out more evidence)
6. Statistical Analysis/ Publication
5. Trial/ Study Design



Process inherently Bayesian!

Slide stolen from Nicky Welton – Summer School *Bayesian methods in health economics*

VoI: Basic ideas

- A new study will provide more data
  - Reducing (or even eliminating?...) uncertainty in a subset of the model parameters
- Update the cost-effectiveness model
  - If optimal decision changes, gain in monetary **net benefit** (NB = utility) from using new optimal treatment
  - If optimal decision doesn't change, no gain in NB
- **Expected** VoI is the average gain in NB

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1. **Expected value of Perfect Information** (EVPI)
   - Value of completely resolving uncertainty in all input parameters to decision model
   - Infinite-sized, long-term follow up trial measuring everything!...
   - Gives an upper bound on the value of the new study – low EVPI suggests we can make our decision based on existing information

VoI: Basic ideas & relevant measures

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2. **Expected value of Partial Perfect Information** (EVPPI)
   - Value of eliminating uncertainty in subset of input parameters to decision model
   - e.g.: Infinite-sized trial measuring relative effects on 1-year survival
   - Useful to identify which parameters are responsible for decision uncertainty

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   - e.g.: Infinite-sized trial measuring relative effects on 1-year survival
   - Useful to identify which parameters are responsible for decision uncertainty

3. **Expected value of Sample Information** (EVSI)
   - Value of reducing uncertainty by conducting a specific study of a given design
   - Can compare the benefits and costs of a study with given design
   - Is the proposed study likely to be a good use of resource? What is the optimal design?

In general, VoI measures are always expressed as something like

VoI measure = Some idealised decision-making process − current decision-making process

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Complexity

- There's no natural upper bound
  - Voi measures are positive, but *how low is low?...*
- Need to account for other factors
  - How much would it cost to get to the point when we can make the idealised decision-making process?
  - Who would that affect?
  - For how long?
  - ...
- Computational & modelling issues
  - You need to know what you're doing (again, modelling **fundamentally** Bayesian)
  - And use suitable tools (basically, never use spreadsheets...)

Expected Value of Perfect Information

	Parameter simulations			
Iteration	π_0	ρ	...	γ
1	0.585	0.3814	...	0.4194
2	0.515	0.0166	...	0.0768
3	0.611	0.1373	...	0.0592
4	0.195	0.7282	...	0.7314
...	...	...	...	...
1000	0.0305	0.204	...	0.558

- Characterise uncertainty in the model parameters
  - In a full Bayesian setting, these are drawings from the posterior distribution of $\boldsymbol{\theta}$
  - In a frequentist setting, these are typically bootstrap draws from a set of univariate ditributions that describe some level of uncertainty around the MLEs

Expected Value of Perfect Information

	Parameter simulations				Expected utility	
Iteration	π_0	ρ	...	γ	$\text{NB}_0(\boldsymbol\theta)$	$\text{NB}_1(\boldsymbol\theta)$
1	0.585	0.3814	...	0.4194	*77480.00*	67795.00
2	0.515	0.0166	...	0.0768	87165.00	*106535.00*
3	0.611	0.1373	...	0.0592	*58110.00*	38740.00
4	0.195	0.7282	...	0.7314	77480.00	*87165.00*
...	...	...	...	...	...	...
1000	0.0305	0.204	...	0.558	48425.00	*87165.00*
				Average	72365.35	*77403.49*

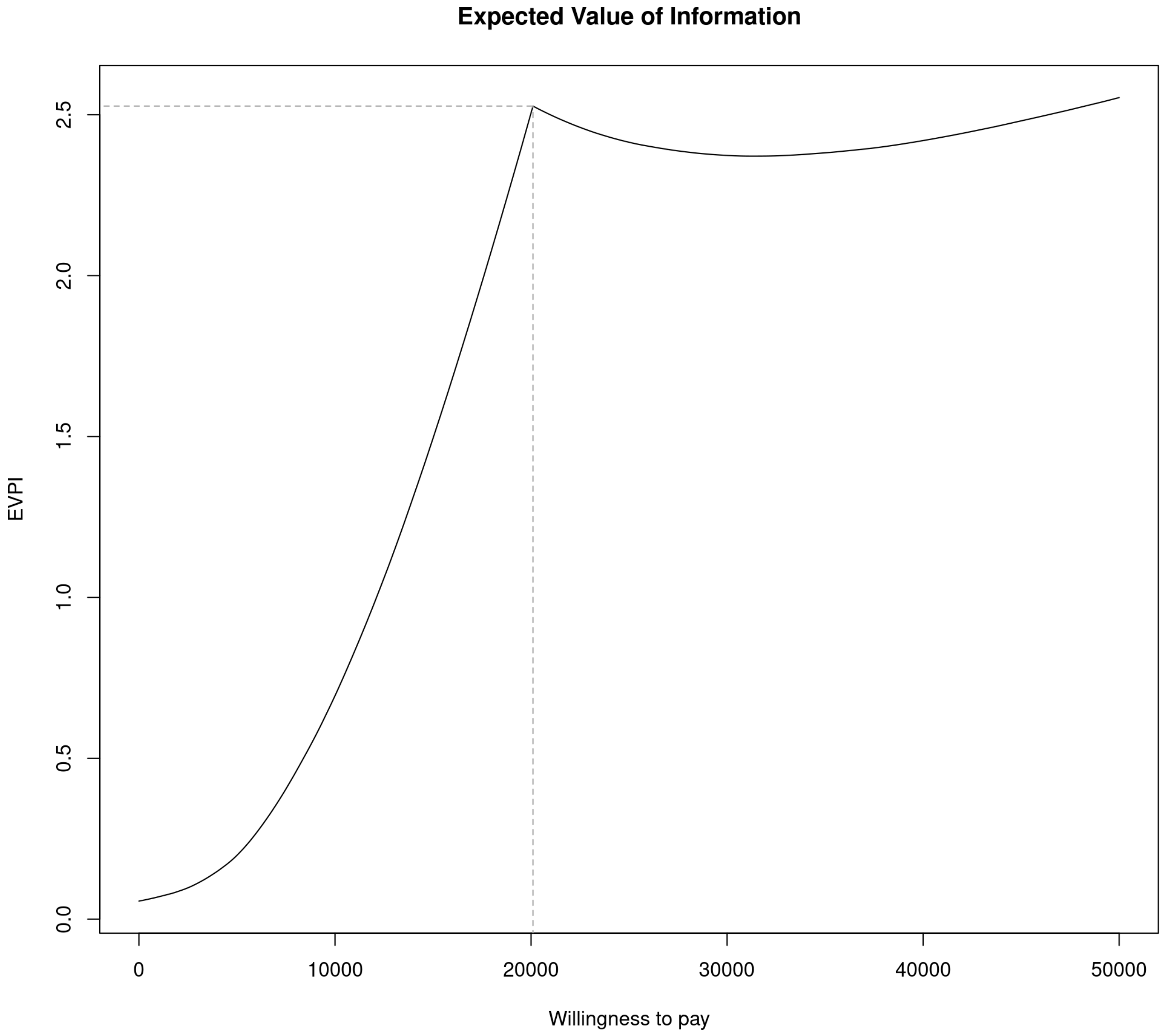
- Uncertainty in the parameters induces a distribution of decisions
  - Typically based on the **net benefits**: $\text{NB}_t(\boldsymbol\theta) = k\mu_{et} - \mu_{ct}$
  - In each parameter configuration can identify the *optimal strategy*
- Averaging over the uncertainty in $\boldsymbol\theta$ provides t^*, the overall optimal decision *given current uncertainty* (= choose the intervention associated with ***highest* expected utility**)

Expected Value of Perfect Information

	Parameter simulations				Expected utility			
Iteration	π_0	ρ	...	γ	$\text{NB}_0(\boldsymbol\theta)$	$\text{NB}_1(\boldsymbol\theta)$	Maximum net benefit	Opportunity loss
1	0.585	0.3814	...	0.4194	*77480.00*	67795.00	77480.00	9685.00
2	0.515	0.0166	...	0.0768	87165.00	*106535.00*	106535.00	0.00
3	0.611	0.1373	...	0.0592	*58110.00*	38740.00	58110.00	19370.00
4	0.195	0.7282	...	0.7314	77480.00	*87165.00*	87165.00	0.00
...	...	...	...	...	...	...	...	...
1000	0.0305	0.204	...	0.558	48425.00	*87165.00*	87165.00	0.00
				Average	72365.35	*77403.49*	**91192.02**	**13788.53**

- **Expected value of "Perfect" Information** (EVPI) summarises uncertainty in the decision
  - Defined as the average Opportunity Loss, or **average maximum expected utility under "perfect" information** — **maximum expected utility overall**:

$$\text{EVPI} = \text{E}_{\boldsymbol\theta}\left[\max_t \text{NB}_t(\boldsymbol\theta)\right] - \max_t \text{E}_{\boldsymbol\theta}\left[\text{NB}_t(\boldsymbol\theta)\right]$$


Expected Value of Information
EVPI
0.0
0.5
1.0
1.5
2.0
2.5
0
10000
20000
30000
40000
50000
Willingness to pay

Expected Value of Partial Perfect Information

- $\boldsymbol{\theta} =$ all the model parameters; can be split into two subsets
  - The "parameters of interest", ϕ, e.g. prevalence of a disease, HRQL measures, length of stay in hospital, ...
  - The "remaining parameters, ψ, e.g. cost of treatment with other established medications, ...
- We are interested in quantifying the value of gaining more information on ϕ, while leaving current level of uncertainty on ψ unchanged

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- First, consider the expected utility (EU) **if** we were able to learn $\boldsymbol\phi$ but not $\boldsymbol\psi$

$$\mathrm{E}_{\boldsymbol\psi\mid\boldsymbol\phi}[\mathrm{NB}_t(\boldsymbol\theta)]$$

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- **If** we knew $\boldsymbol\phi$ perfectly, best decision = the maximum of this EU

$$\max_t \mathsf{E}_{\boldsymbol\psi|\boldsymbol\phi}[\mathsf{NB}_t(\boldsymbol\theta)]$$

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- Of course, we cannot know ϕ **perfectly**, so take the expected value

$$\mathrm{E}_{\phi}\left[\max_t \mathrm{E}_{\psi|\phi}[\mathrm{NB}_t(\boldsymbol\theta)]\right]$$

Expected Value of Partial Perfect Information

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- Of course, we cannot know $\boldsymbol\phi$ **perfectly**, so take the expected value
- And compare this with the **maximum expected utility overall**

$$\mathrm{E}_{\boldsymbol\phi}\left[\max_t \mathrm{E}_{\boldsymbol\psi|\boldsymbol\phi}[\mathrm{NB}_t(\boldsymbol\theta)]\right] - \max_t \mathrm{E}_{\boldsymbol\theta}[\mathrm{NB}_t(\boldsymbol\theta)]$$

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- This is the EVPPI

$$\text{EVPPI} = \text{E}_{\boldsymbol\phi}\left[\max_t \text{E}_{\boldsymbol\psi|\boldsymbol\phi}[\text{NB}_t(\boldsymbol\theta)]\right] - \max_t \text{E}_{\boldsymbol\theta}[\text{NB}_t(\boldsymbol\theta)]$$

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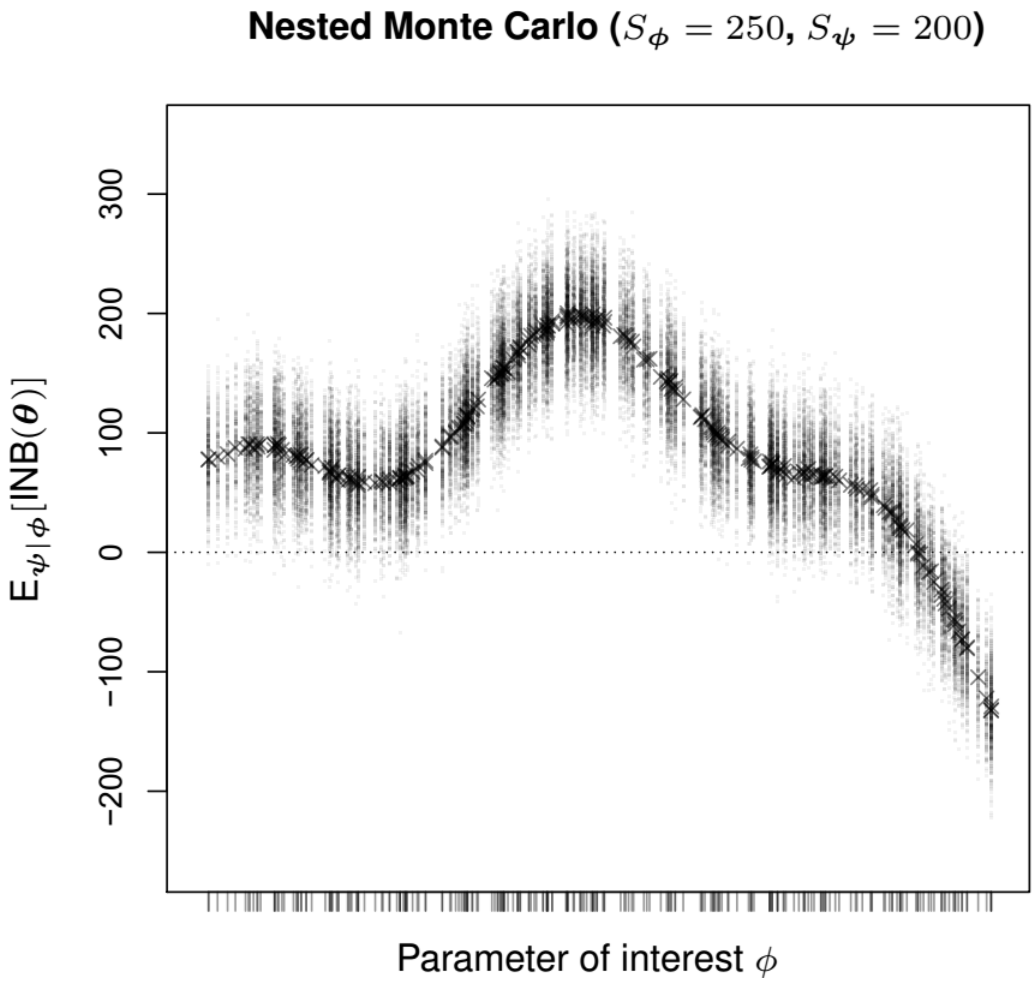
$$\text{EVPPI} = \mathrm{E}_{\phi}\left[\max_t \mathrm{E}_{\psi|\phi}[\mathrm{NB}_t(\boldsymbol\theta)]\right] - \max_t \mathrm{E}_{\boldsymbol\theta}[\mathrm{NB}_t(\boldsymbol\theta)]$$

- That is the difficult part!
  - Can do nested Monte Carlo, but takes for ever to get accurate results
  - Recent methods based on **GAMs/Gaussian Process regression/spatial modelling** very efficient and quick!

Strong et al (2014) and Heath et al (2016)

Assuming there are only two interventions, can consider $\text{IB}(\boldsymbol\theta) = \text{NB}_1(\boldsymbol\theta) - \text{NB}_0(\boldsymbol\theta)$



Slide stolen from Mark Strong – Summer School *Bayesian methods in health economics*

EVPPI – Brute force/nested MC

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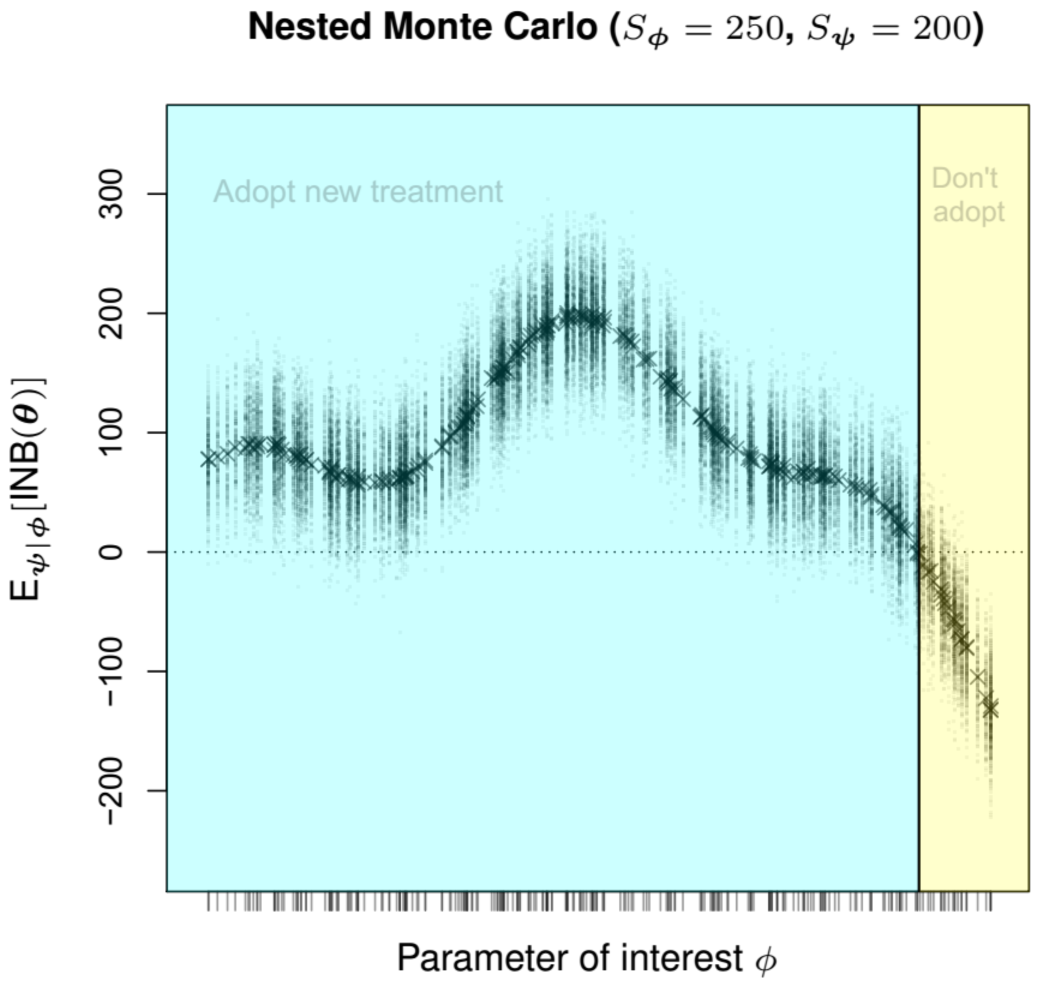


Can model as a **regression** problem

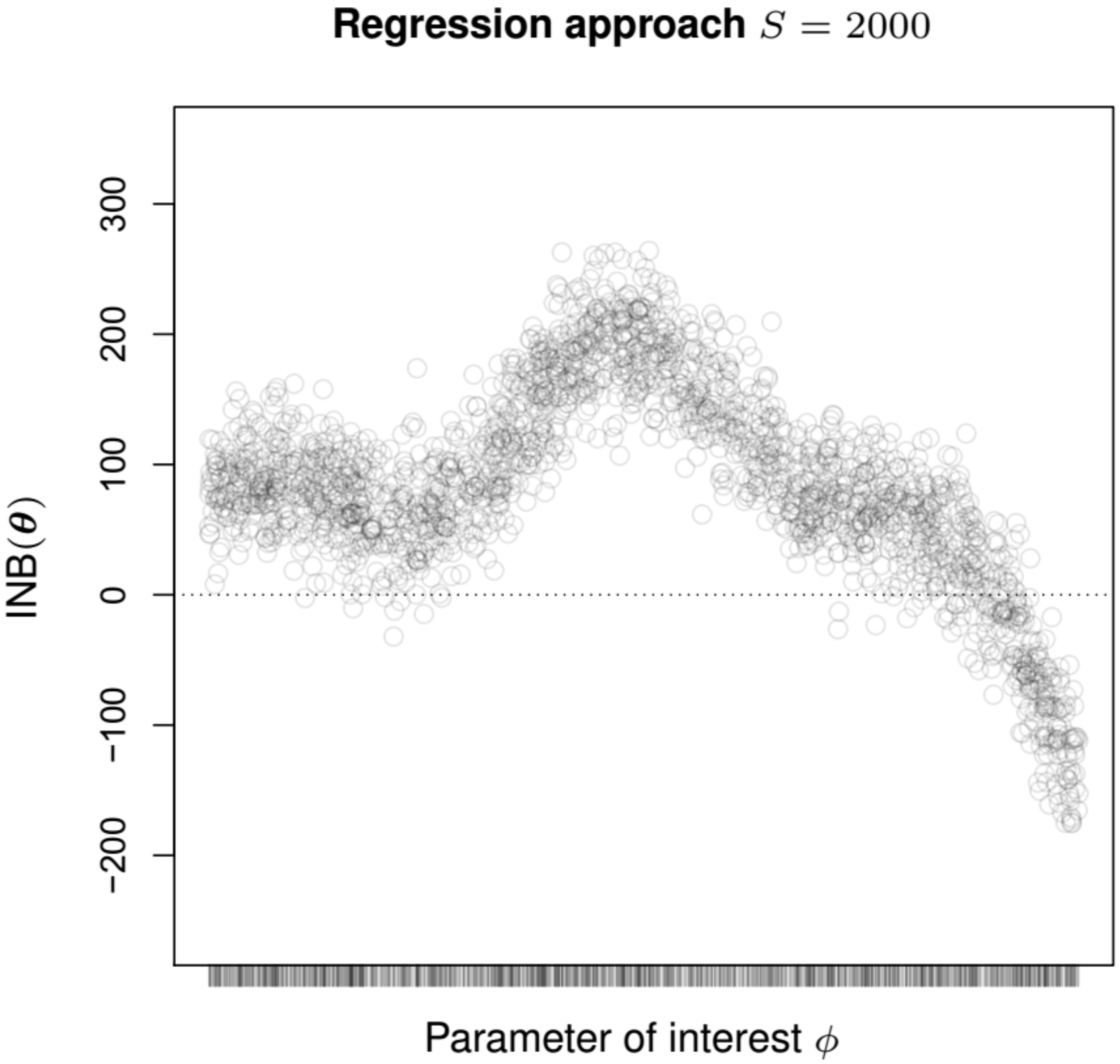
$$\begin{aligned} \text{NB}_t(\boldsymbol\theta) =& \text{E}_{\boldsymbol\psi|\boldsymbol\theta}[\text{NB}_t(\boldsymbol\theta)] + \varepsilon, \qquad \text{with } \varepsilon \sim \text{Normal}(0,\sigma^2_\varepsilon) \\ =& g(\boldsymbol\phi) + \varepsilon \end{aligned}$$

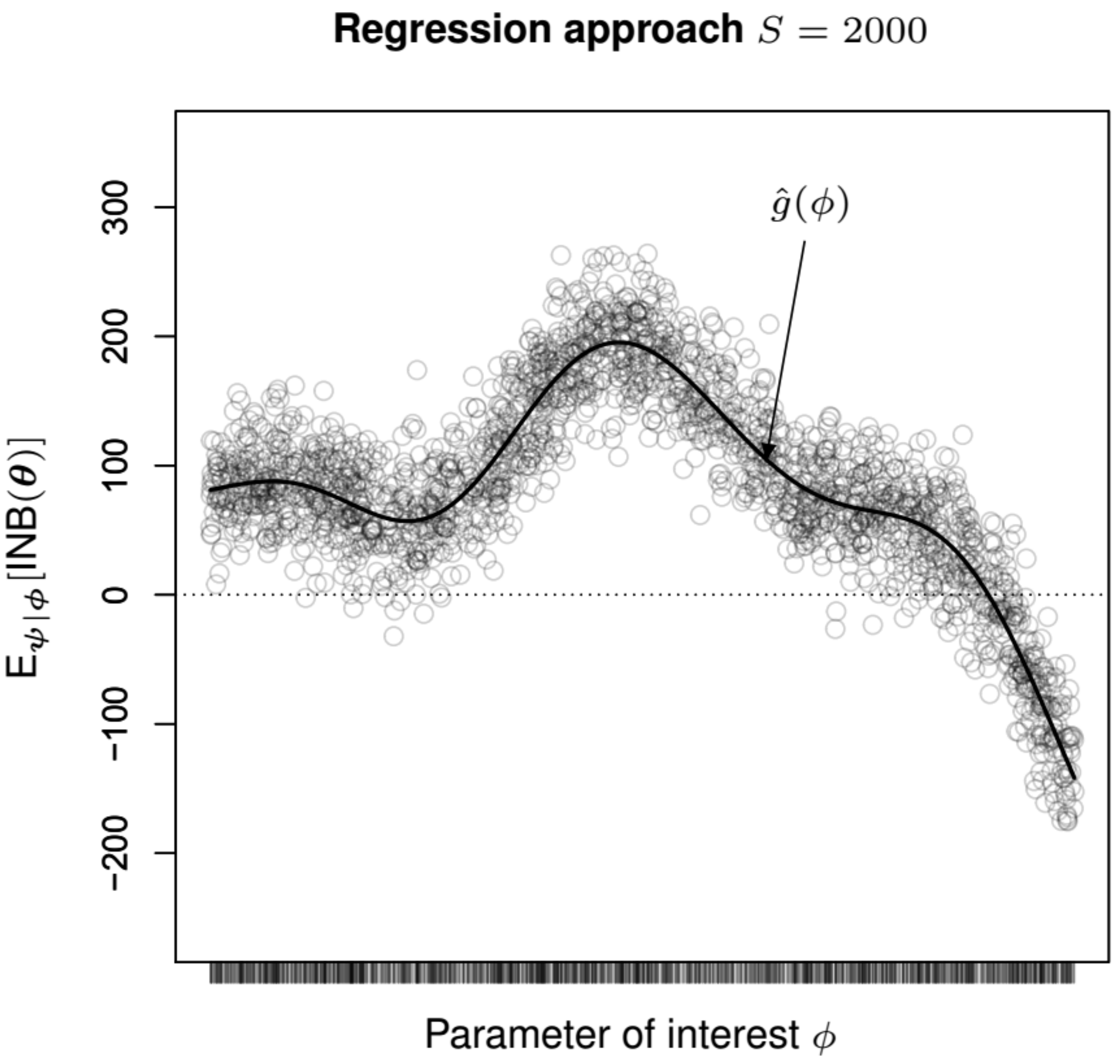
"Data"

- **Simulations** for $\text{NB}_t(\boldsymbol\theta)$ as "response"
- **Simulations** for $\boldsymbol\phi$ as "covariates"
- **NB**: Only need S data points (=PSA simulations), instead of $S_{\boldsymbol\phi} \times S_{\boldsymbol\psi}$!

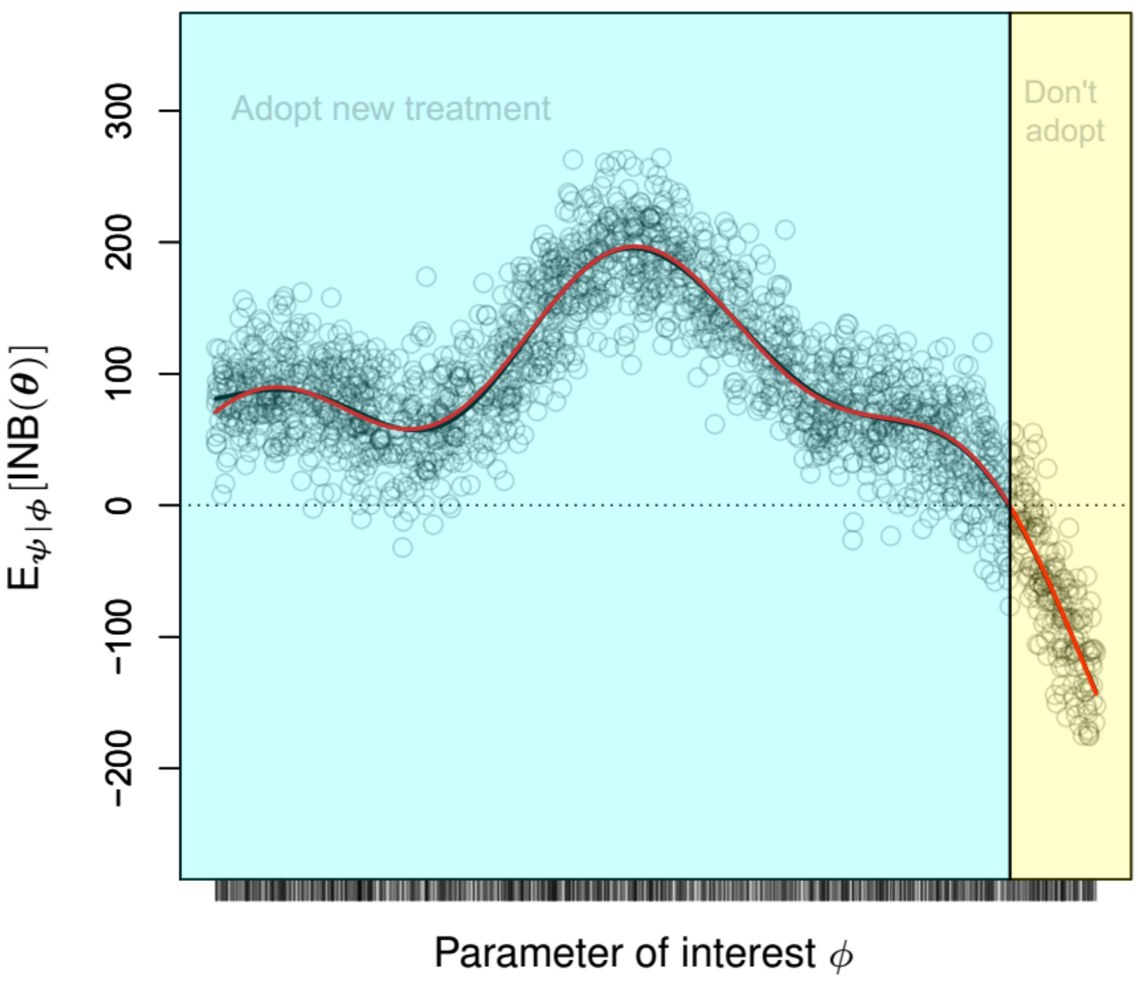
	Parameter simulations ('covariates')				'Responses'	
Iteration	π_0	ρ	...	γ	$\text{NB}_0(\boldsymbol\theta)$	$\text{NB}_1(\boldsymbol\theta)$
1	0.585	0.3814	...	0.4194	77480	67795
2	0.515	0.0166	...	0.0768	87165	106535
3	0.611	0.1373	...	0.0592	58110	38740
4	0.195	0.7282	...	0.7314	77480	87165
...	...	...	...	...	...	...
S	0.0305	0.204	...	0.558	48425	87165

EVPPI – model as a regression problem...




Regression approach $S = 2000$
$\hat{g}(\phi)$
$E_{\psi|\phi}[\text{INB}(\boldsymbol\theta)]$
300
200
100
0
−100
−200
Parameter of interest ϕ

Regression approach $S = 2000$ (True relationship in red)



- Once the functions $g_t(\phi)$ are estimated, can approximate

$$\begin{aligned}\text{EVPPI} &= \mathsf{E}_{\boldsymbol\phi}\left[\max_t \mathsf{E}_{\boldsymbol\psi\mid\boldsymbol\phi}[\mathsf{NB}_t(\boldsymbol\theta)]\right] - \max_t \mathsf{E}_{\boldsymbol\theta}[\mathsf{NB}_t(\boldsymbol\theta)] \\ &\approx \frac{1}{S}\sum_{s=1}^{S}\max_t \hat{g}_t(\boldsymbol\phi_s) - \max_t \frac{1}{S}\sum_{s=1}^{S}\hat{g}_t(\boldsymbol\phi_s)\end{aligned}$$

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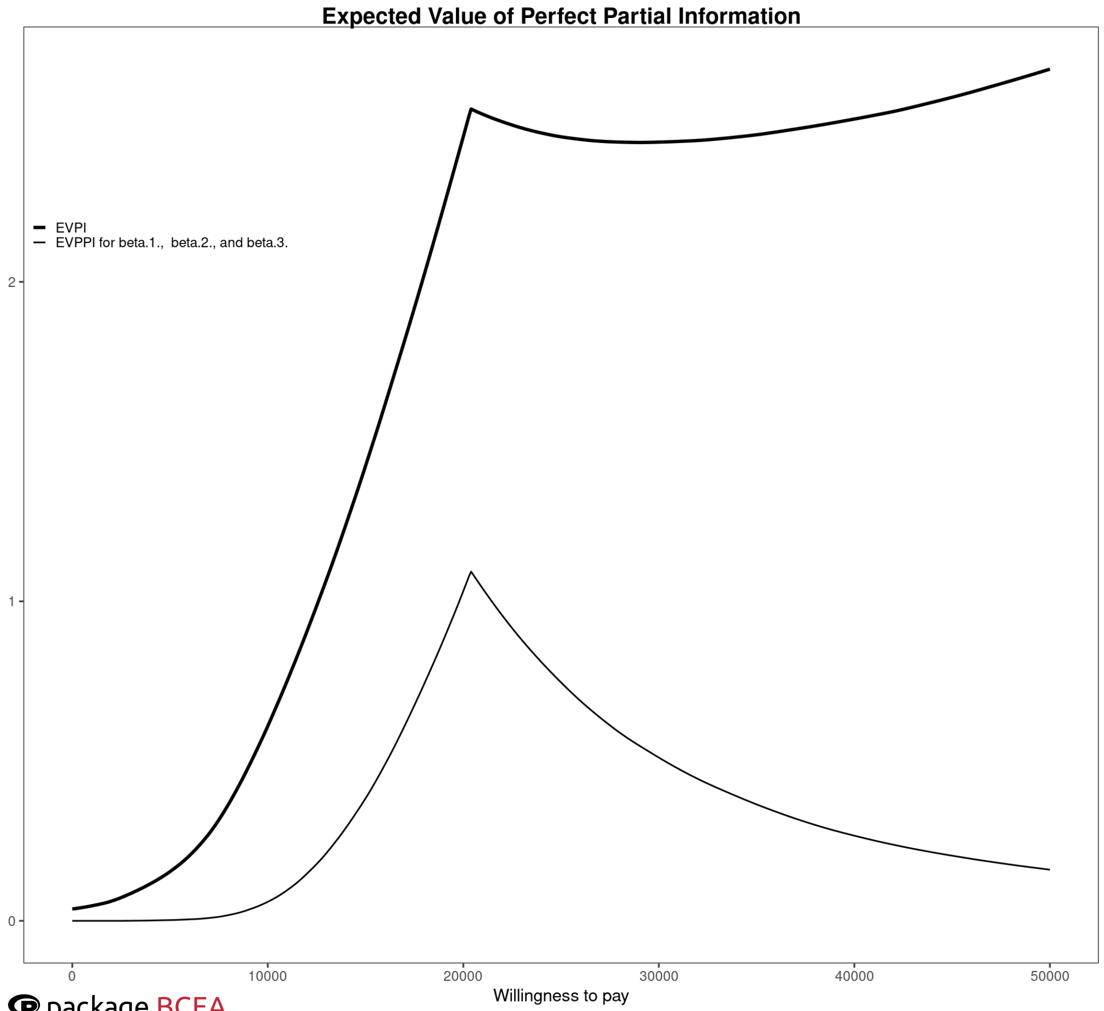
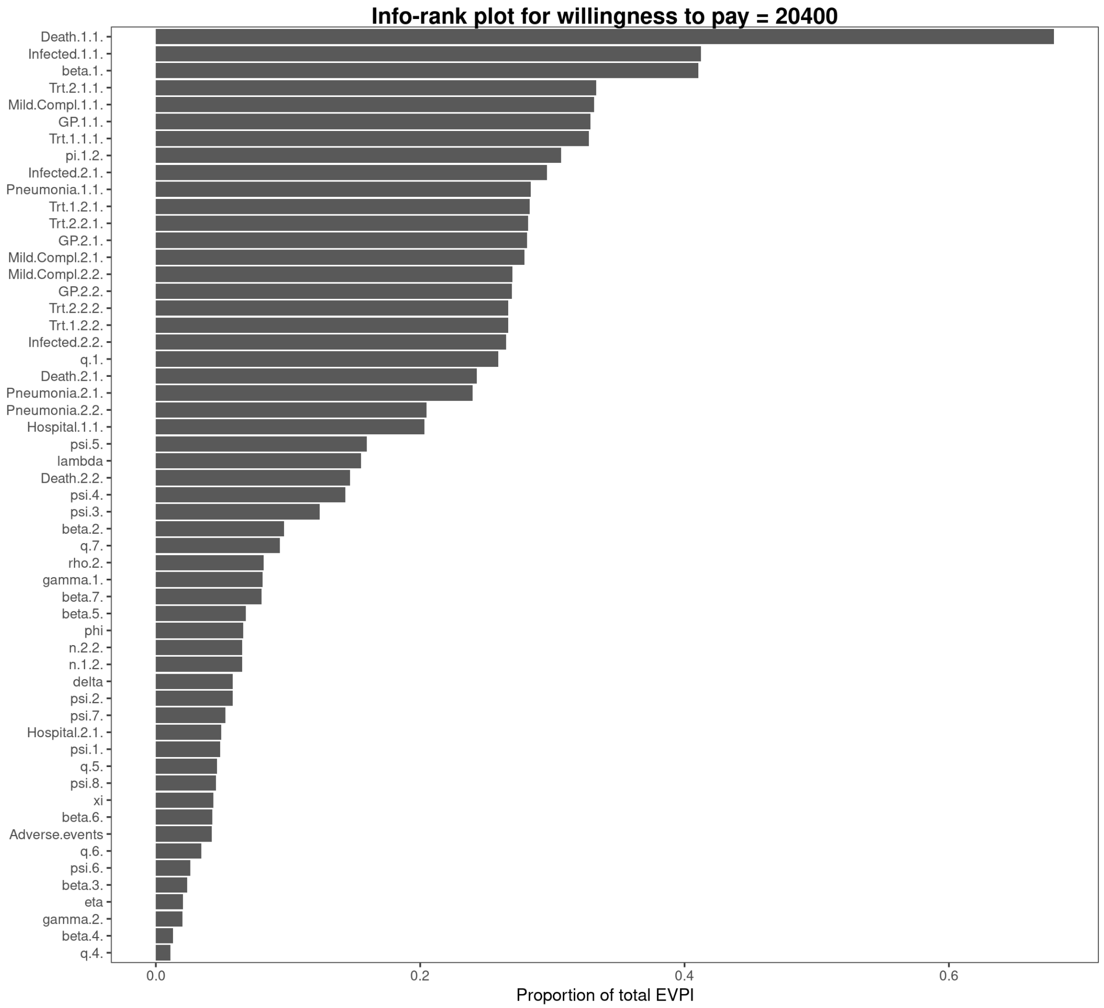
- **NB**: $g_t(\phi)$ can be complex, so need to use flexible regression methods
  - **GAMs**: $g_t(\phi) = \sum_{q=1}^{Q_\phi} h_t(\phi_{sq})$ with $h_t(\cdot) =$ smooth functions (cubic polynomials)
  - very fast, but only if number of important parameters $Q_\phi \leq 5$ (interactions increase model size exponentially)
  - If $Q_\phi > 5$ then use Gaussian Process regression (GPR)
    - Strong et al: original GPR method
    - Heath et al: based on spatial modelling; can be more computationally efficient
- Other methods based on alternative approaches
  - Most are implemented in the R package BCEA (see also: https://github.com/giabaio/BCEA)

Summarising PSA + Research priority





package BCEA

https://github.com/giabaio/BCEA

https://egon.stats.ucl.ac.uk/projects/BCEAweb https://savi.shef.ac.uk/SAVI/

The University Of Sheffield. (http://www.sheffield.ac.uk/) SAVI - Sheffield Accelerated

Value of Information

Release version 2.2.0 (2021-06-04)

Home About your model Import files Check upload PSA Results EVPI EVPPI single parameters EVPPI groups Risk Analysis Report

About us

What SAVI does

Using **only** PSA results from your model

In a matter of seconds from the SAVI online application you can generate:

1. Standardised assessment of uncertainty (C-E planes and CEACs)
2. Overall EVPI per patient, per jurisdiction per year and over your decision relevance horizon
3. Expected Value of Perfect Parameter Information (EVPPI) for single and groups of parameters

Disclaimer: This application is based on peer-reviewed statistical approximation methods. It comes with no warranty and should be utilised at the user's own risk (see here (https://raw.githubusercontent.com/Sheffield-Accelerated-VoI/SAVI/master/DISCLAIMER.txt)). The underlying code (https://github.com/Sheffield-Accelerated-VoI/SAVI) is made available under the BSD 3-clause license (https://raw.githubusercontent.com/Sheffield-Accelerated-VoI/SAVI/master/LICENSE.txt).

If you use SAVI in your work please cite our paper

Strong M, Oakley JE, Brennan A. Estimating multi-parameter partial Expected Value of Perfect Information from a probabilistic sensitivity analysis sample: a non-parametric regression approach. *Medical Decision Making*. 2014;**34(3)**:311-26. Available open access here. (http://mdm.sagepub.com/content/34/3/311)

The SAVI process has 4 steps (using the TABS from left to right)

Contact Us

For any queries or to report a bug please send an email to savi@sheffield.ac.uk (mailto:savi@sheffield.ac.uk)

News

SAVI is now available as an R package, allowing you to run SAVI directly on your own machine. You can download instructions here. (https://www.shef.ac.uk/polopoly_fs/1.511325!/file/Instructio
package.txt)

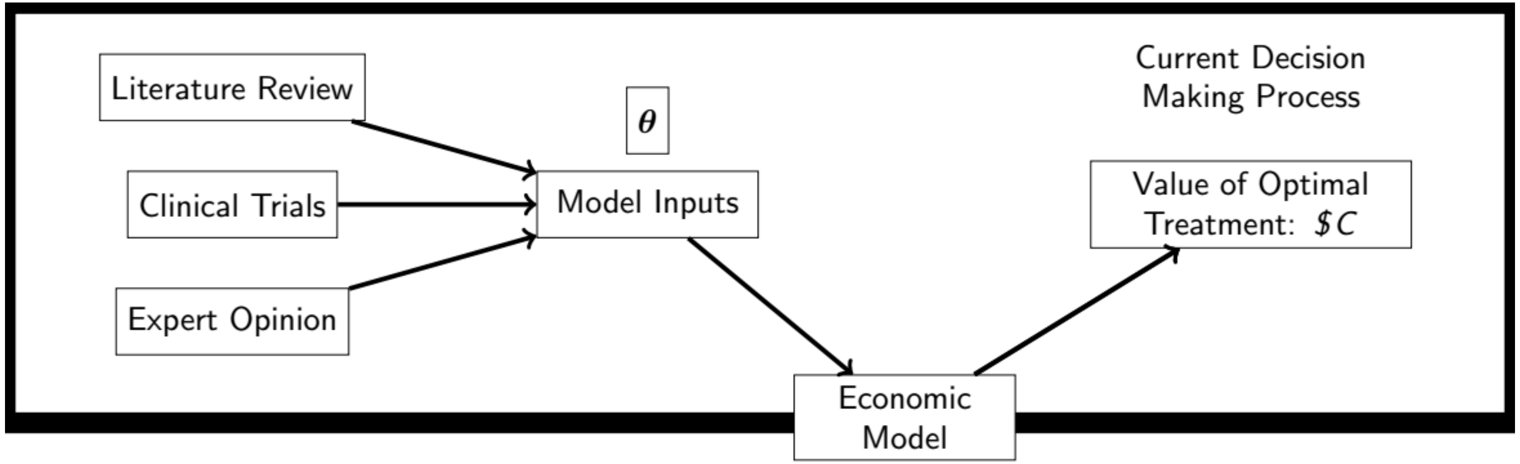
New features and bug fixes

New for version 2.2.0

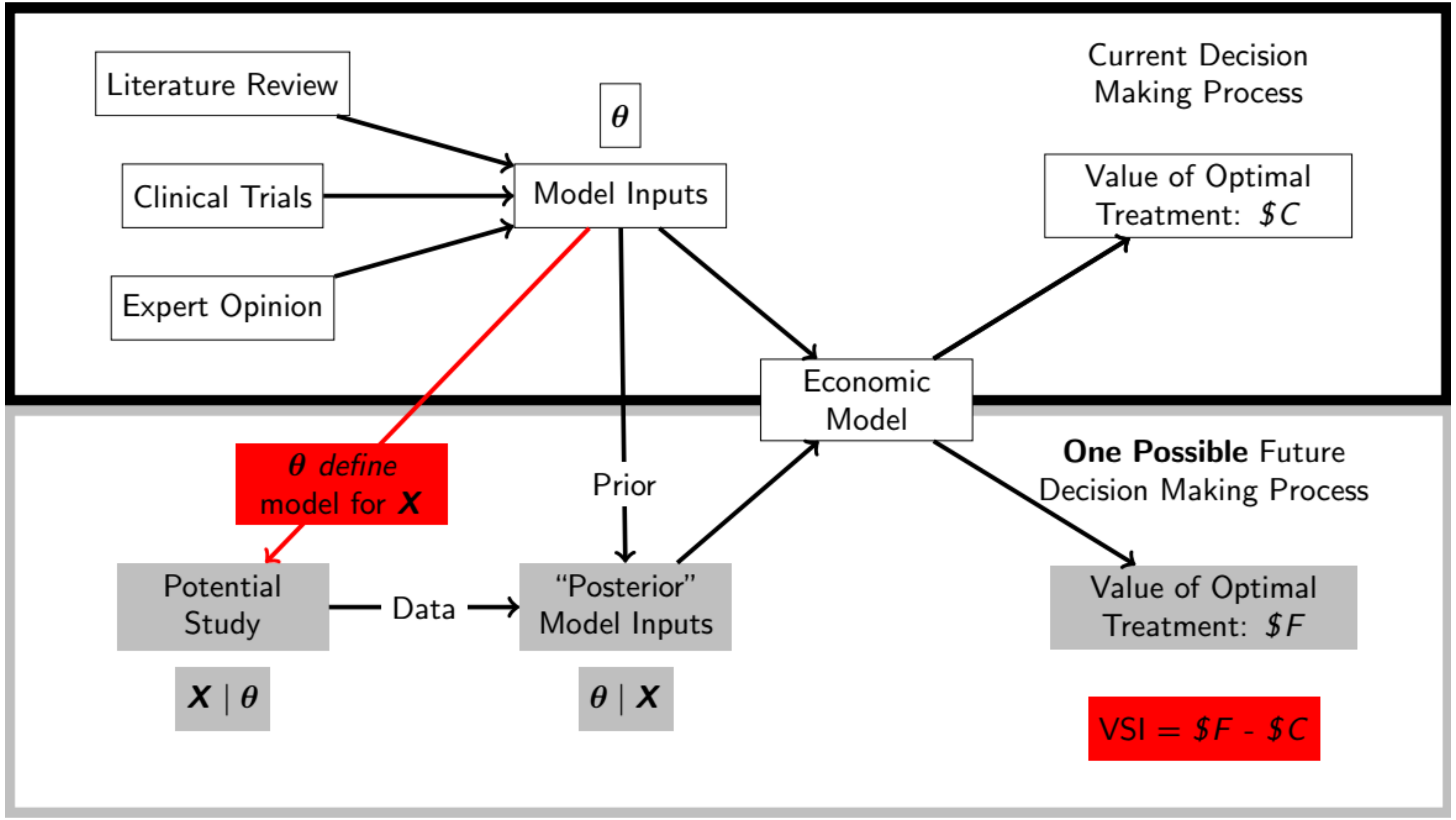
SAVI now has a new web address https://savi.shef.ac.uk/SAVI/ (https://savi.shef.ac.uk/SAVI/)

This means that traffic to and from SAVI is now

Expected value of **sample** information



Expected value of **sample** information



Stolen from various presentations by Anna Heath

Expected value of **sample** information

Jackson et al (2021)

- EVSI measures the value of reducing uncertainty by running a study of **a given design**

$$\text{EVSI} = \text{E}_{\boldsymbol{X}} \left[\max_t \underbrace{\text{E}_{\boldsymbol{\theta}|\boldsymbol{X}} \left[\text{NB}_t(\boldsymbol{\theta}) \right]}_{\substack{\uparrow \\ \text{Value of decision based} \\ \text{on sample information} \\ \text{(for a given study design)}}} \right] - \max_t \underbrace{\text{E}_{\boldsymbol{\theta}} \left[\text{NB}_t(\boldsymbol{\theta}) \right]}_{\substack{\uparrow \\ \text{Value of decision based} \\ \text{on current information}}}$$

- Can compare the benefits and costs of a study with given design
  - To see if a proposed study likely to be a good use of resources
  - To find the optimal study design

Expected value of **sample** information

Jackson et al (2021)

- EVSI measures the value of reducing uncertainty by running a study of **a given design**

$$\text{EVSI} = \text{E}_{\boldsymbol X}\left[\max_t \text{E}_{\boldsymbol\theta|\boldsymbol X}\left[\text{NB}_t(\boldsymbol\theta)\right]\right] - \max_t \text{E}_{\boldsymbol\theta}\left[\text{NB}_t(\boldsymbol\theta)\right]$$

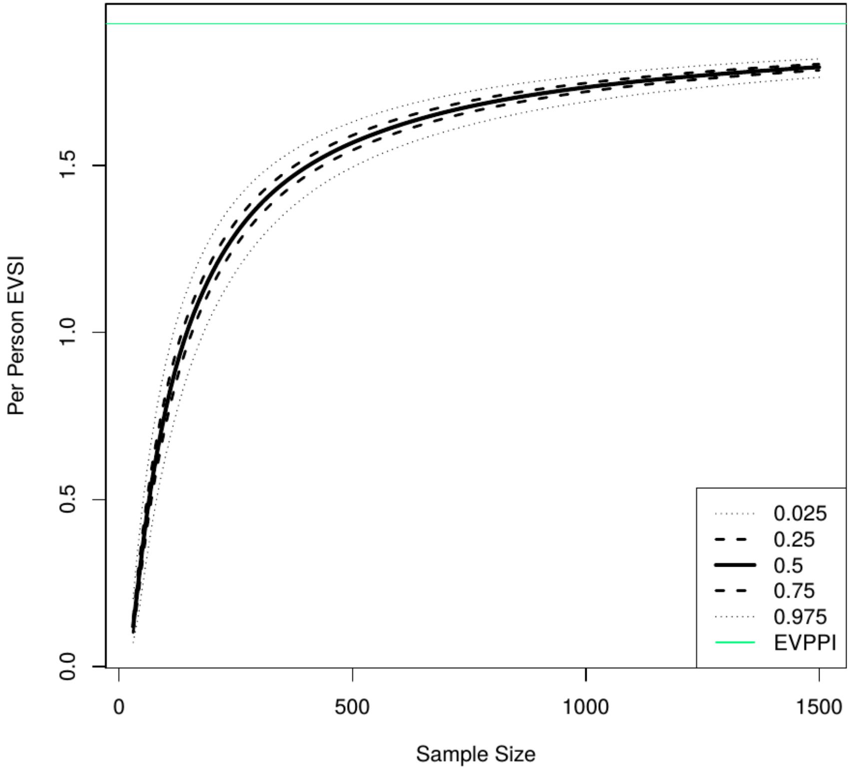
↑ Value of decision based on **sample** information (for a given study design)

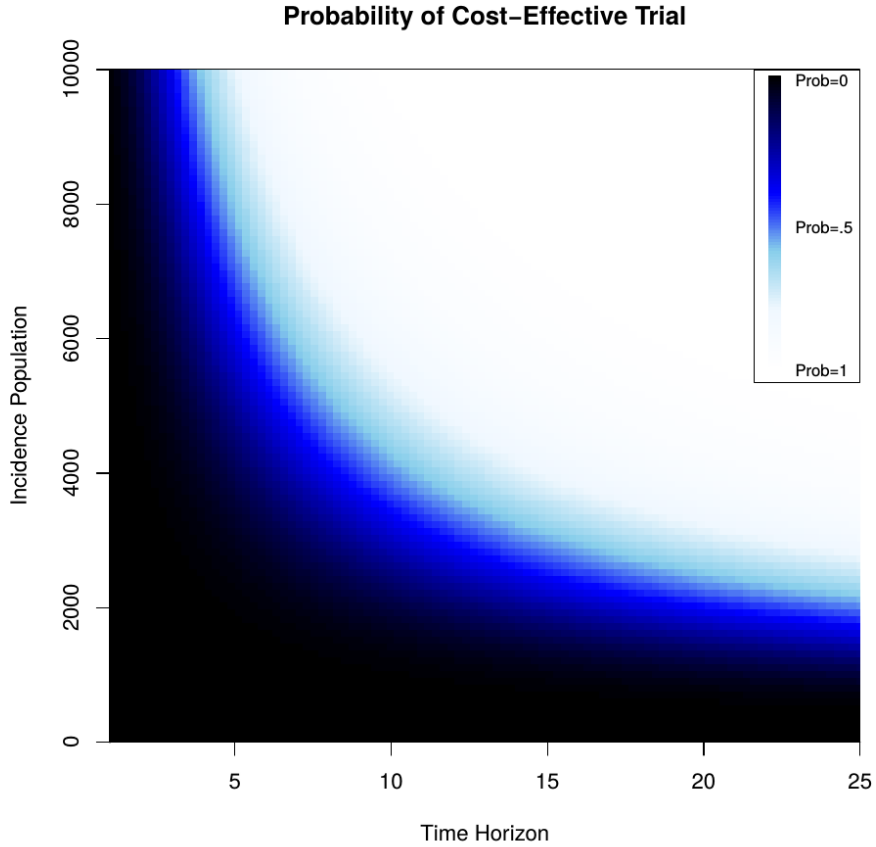
↑ Value of decision based on **current** information

- Can compare the benefits and costs of a study with given design
  - To see if a proposed study likely to be a good use of resources
  - To find the optimal study design
- Computationally complex
  - Requires specific knowledge of the model for (future/hypothetical) data collection
- Again, recent methods have improved efficiency

  Heath et al (2021)
  - Regression-based (Strong et al, 2015)
  - Importance Sampling (Menzies et al, 2016)
  - Gaussian approximation (Jalal et al, 2015; Jalal and Alarid-Escudero, 2018)
  - Moment matching (Heath et al, 2018)
- Can be used to drive design of new study (eg sample size calculations)

Expected value of **sample** information



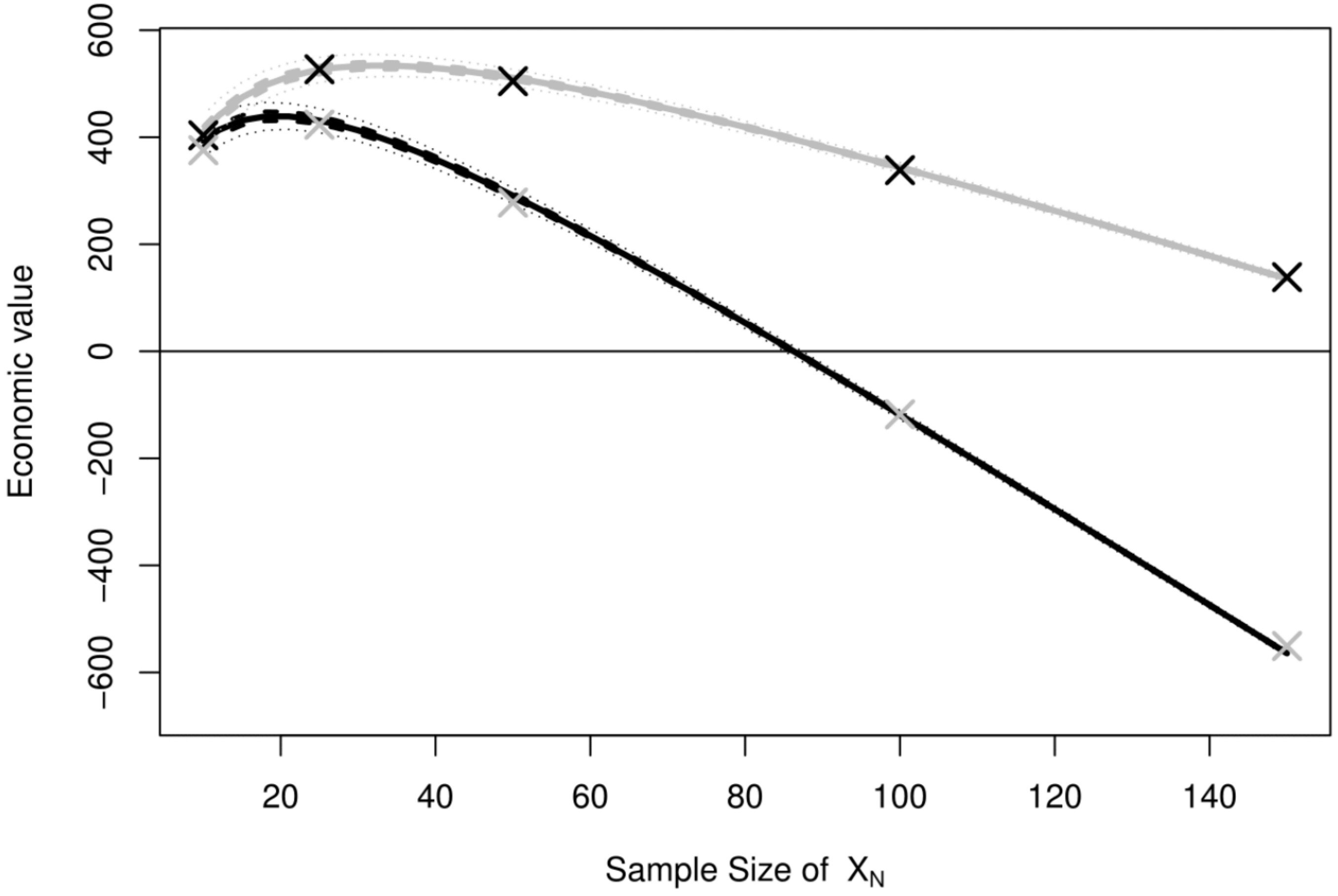


https://github.com/giabaio/EVSI and https://github.com/chjackson/voi

https://egon.stats.ucl.ac.uk/projects/EVSI

Heath et al (2019)

Expected value of **sample** information



NICE HTA evaluation methods update (2021)

> *2.16. The use of Expected Value of Perfect Information (EVPI) will **not** be adopted into the NICE methods. Stakeholders raised concerns about this proposal and the majority disagreed with it. It was noted that the added value of EVPI and how it would be used in decision-making was unclear as experiences from other countries suggested that its added value to decision making is minimal. There were concerns that it would add complexity to decision making, and the additional burden for analysts and reviewers may not be worth it. On the other hand, some stakeholders argued that the proposal did not go far enough and should include expected value of partially perfect information (EVPPI) and expected value of sample information (EVSI).*

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- Push from industrial representatives, despite attempts at clarifying/simplyfing concepts/guidelines
- CADHT actually say

> *When the decision problem includes consideration of further research to inform future decisions, a value-of-information analysis should be undertaken as part of the reference case. [...] To identify these critical values and correctly quantify the impact of a parameter taking a specific value (on both the probability of an intervention being cost-effective and the expected net benefit), recent methodological work suggests that a two-stage expected value of perfect parameter information analysis may be useful*

Conclusions

- HTA is fundamentally based on statistical modelling – and statisticians should be much more heavily involved in the whole process
  - More modellers with stronger statistical background – often (**though not always!**) use of suboptimal tools is a red flag for lack of necessary sophistication in statistical modelling
  - More statisticians developing methods, sitting on panels and creating critical mass

Conclusions

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  – More modellers with stronger statistical background – often (**though not always!**) use of suboptimal tools is a red flag for lack of necessary sophistication in statistical modelling
  – More statisticians developing methods, sitting on panels and creating critical mass

- VoI methods can be very helpful
  – The can address multiple questions, including research prioritisation
  – Vital in issues such as managed entry/conditional reimbursment

- Still a battle...