11. Introduction to Value of Information

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Bayesian Methods in Health Economics, Lausanne

Summary

- Motivating Value of Information (VoI) approach
- Summarising uncertainty and PSA
- Research priorities

References

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

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

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

Knowledge is power?

(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**!

Value of Information (VoI)

(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⇒**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⇒**probably should think about it...**!

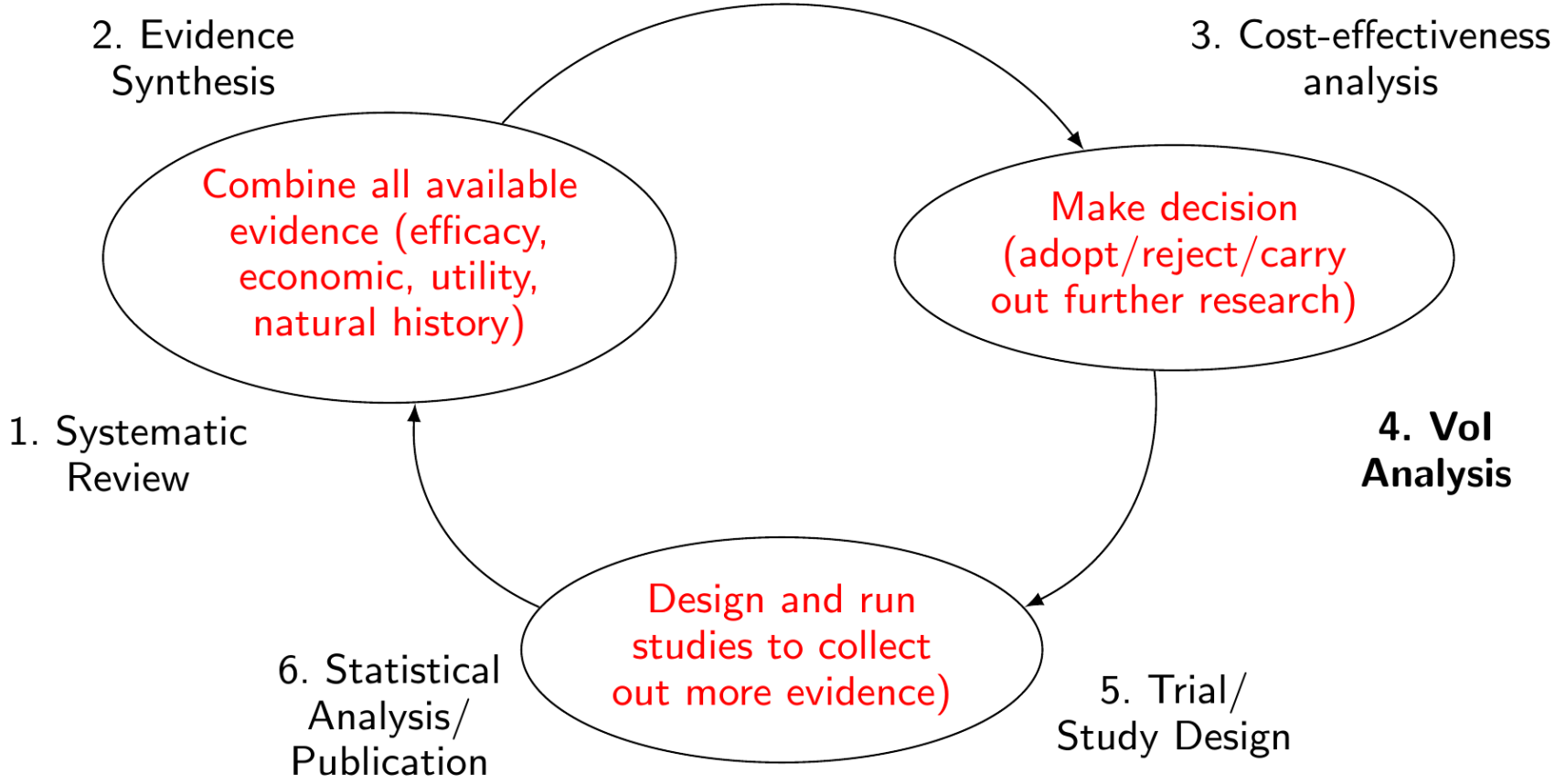
Decisions with uncertainty

- Net Benefit depends on:
  - Relative treatment efficacy (e.g. meta-analysis)
  - Relative treatment efficacy (e.g. meta-analy Natural history / disease progression
  - Utility (quality of life)
  - Economic parameters (costs)

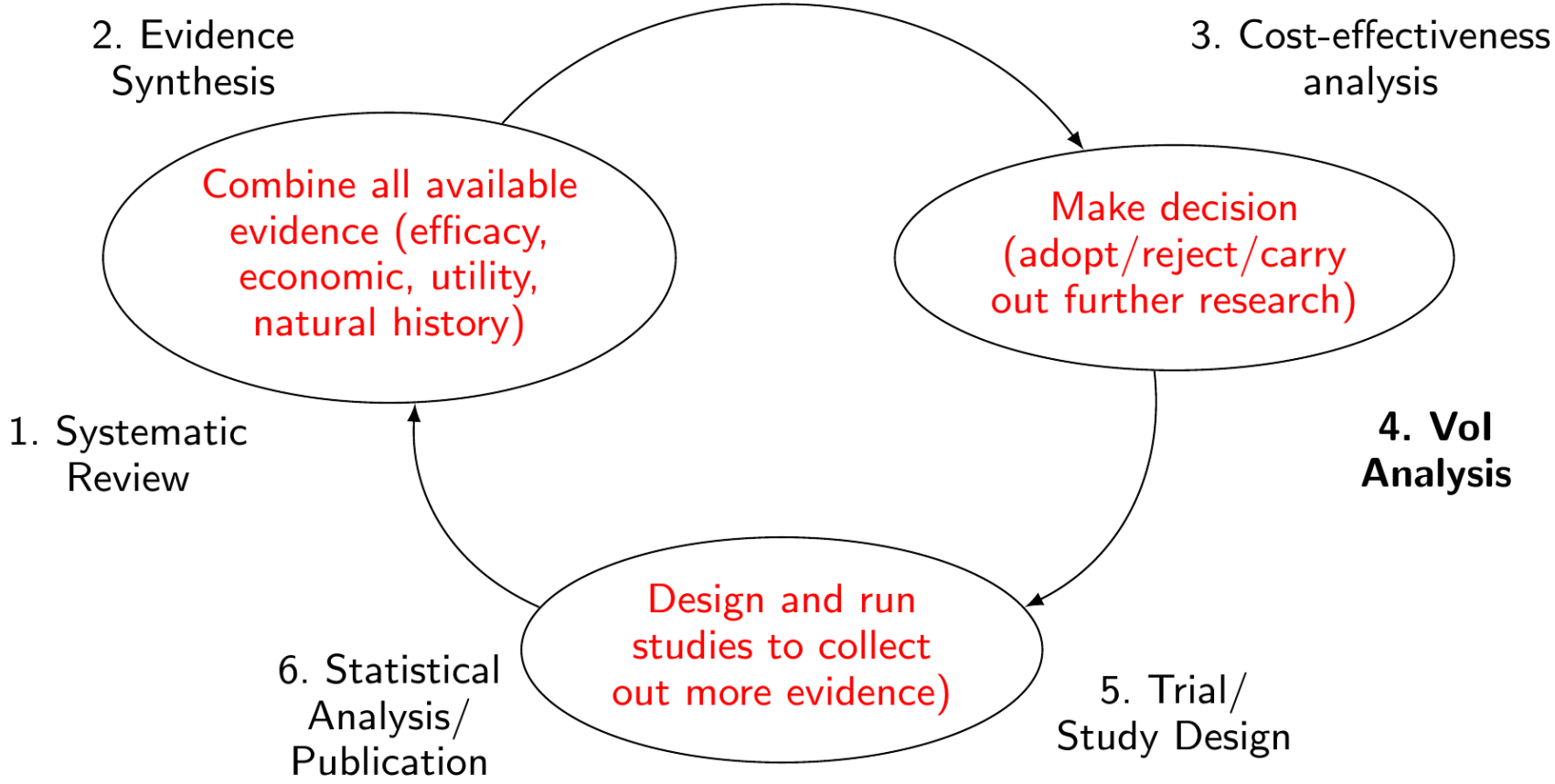
- Uncertainty may exist on all these inputs
  - *Parameter* uncertainty

- Translates into uncertainty in expected NB
  - *Decision* uncertainty
  - Are we happy to make a decision currently?
  - Should we consider collecting more info?

Evidence based decision-making and VoI



Evidence based decision-making and VoI



Process inherently Bayesian!

Slide stolen from Nicky Welton

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

VoI: Basic ideas & relevant measures

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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

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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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  - Reducing (or even eliminating?...) uncertainty in a subset of the model parameters
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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?

VoI: Basic ideas & relevant measures

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**:

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

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- $\left[\max_t \text{NB}_t(\boldsymbol{\theta})\right]$: Value of decision if we knew $\boldsymbol{\theta}$
- $\max_t \text{E}_{\boldsymbol{\theta}}\left[\text{NB}_t(\boldsymbol{\theta})\right]$: Value of decision based on current information

Summarising uncertainty analysis (PSA)

Expected Value of Perfect Information

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Useful to rewrite as

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

where t^* maximises $\text{E}_{\boldsymbol{\theta}}\left[\text{NB}_t(\boldsymbol{\theta})\right]$, based on current information

- $\left[\max_t \text{NB}_t(\boldsymbol{\theta}) - \text{NB}_{t*}(\boldsymbol{\theta})\right]$: Opportunity lost from using t^* instead of the optimal t for $\boldsymbol{\theta}$

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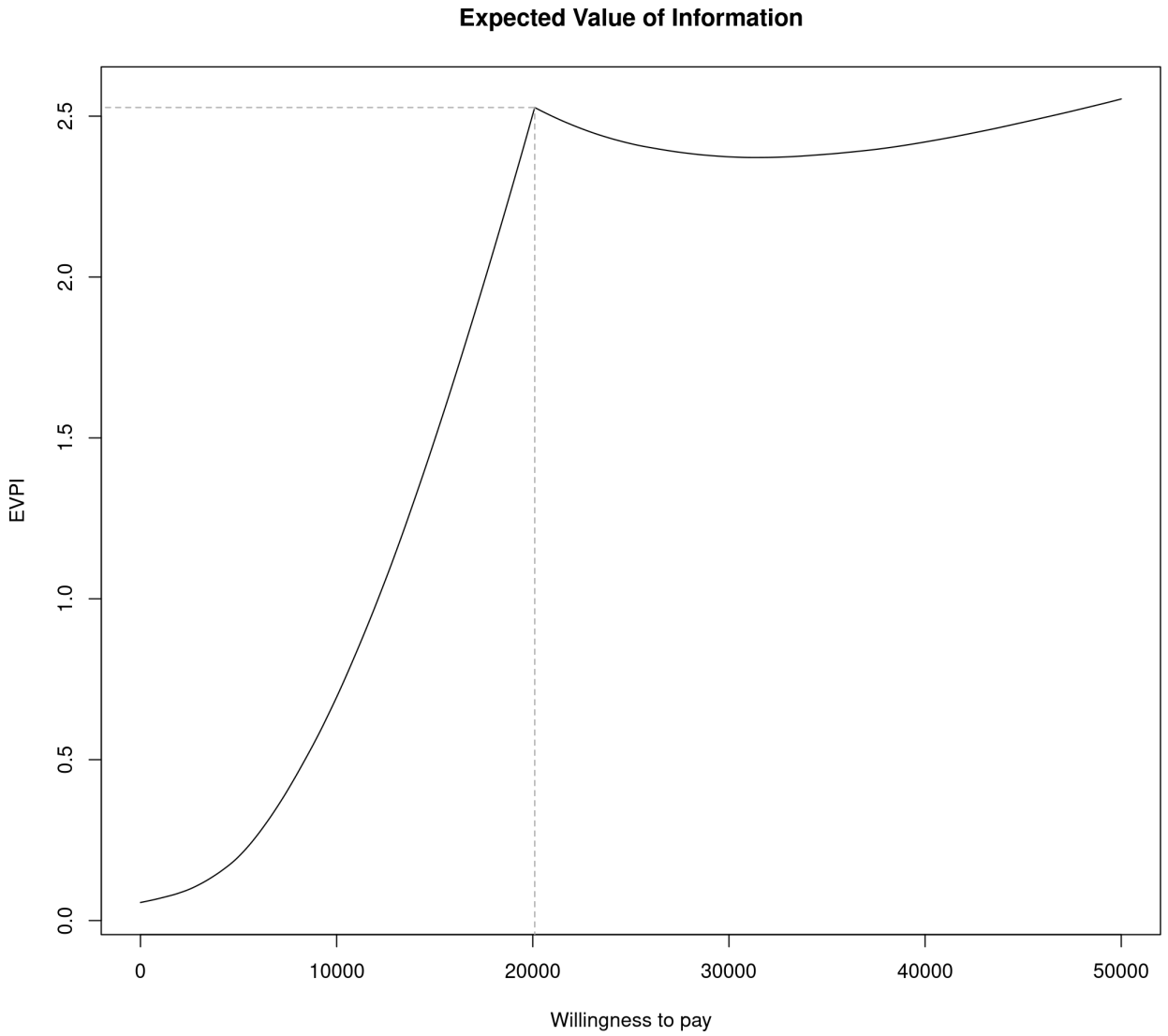
- $\left[\max_t \text{NB}_t(\boldsymbol{\theta}) - \text{NB}_{t*}(\boldsymbol{\theta})\right]$: Opportunity lost from using t^* instead of the optimal t for $\boldsymbol{\theta}$

Golden rule of Value of Information

Information only has value if it changes your decision

Summarising uncertainty analysis (PSA)



Example – HIV screening decision model

Objectives

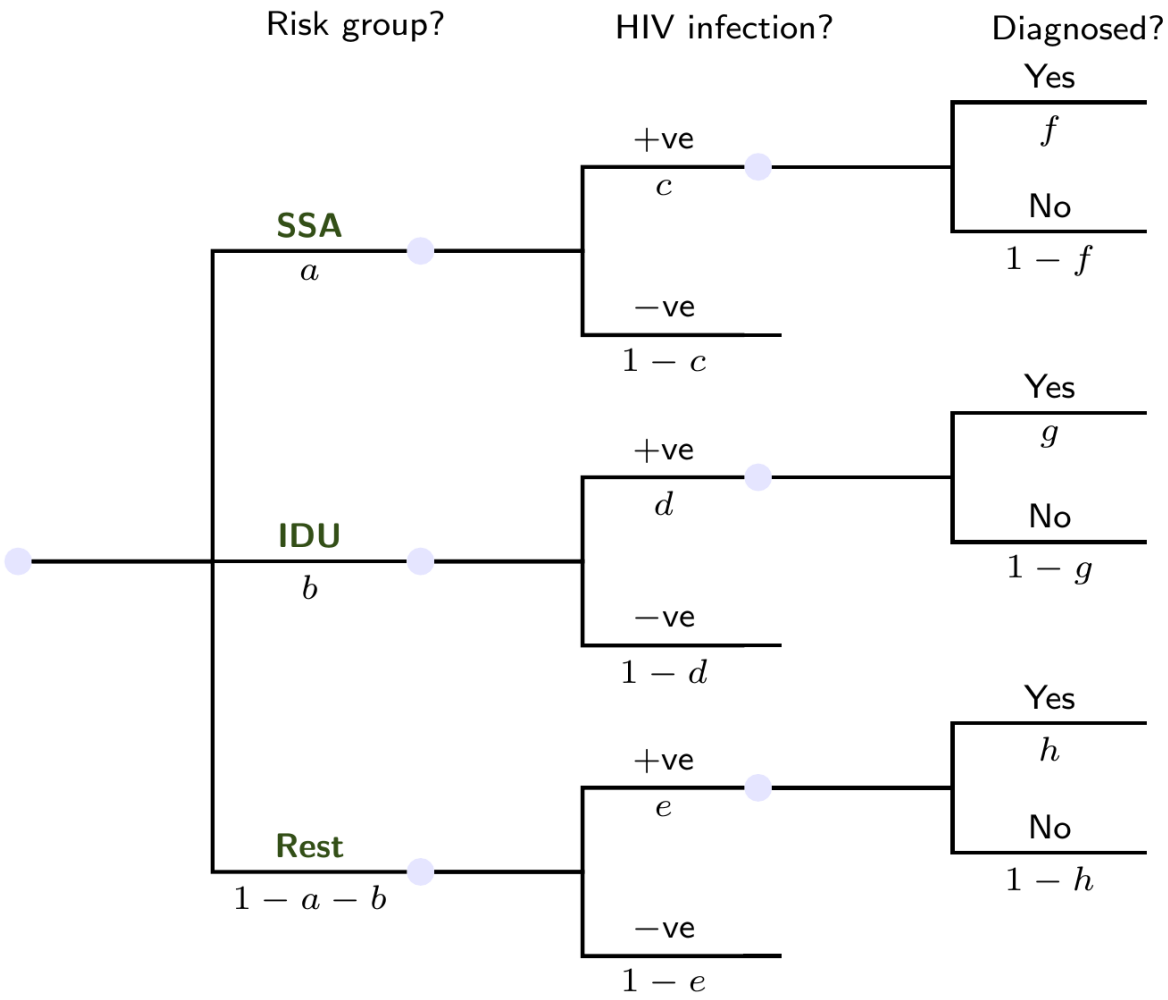
- To investigate the net benefit of a universal screening over targeted screening for HIV

Design of the study

- Multi-parameter evidence synthesis of observational studies

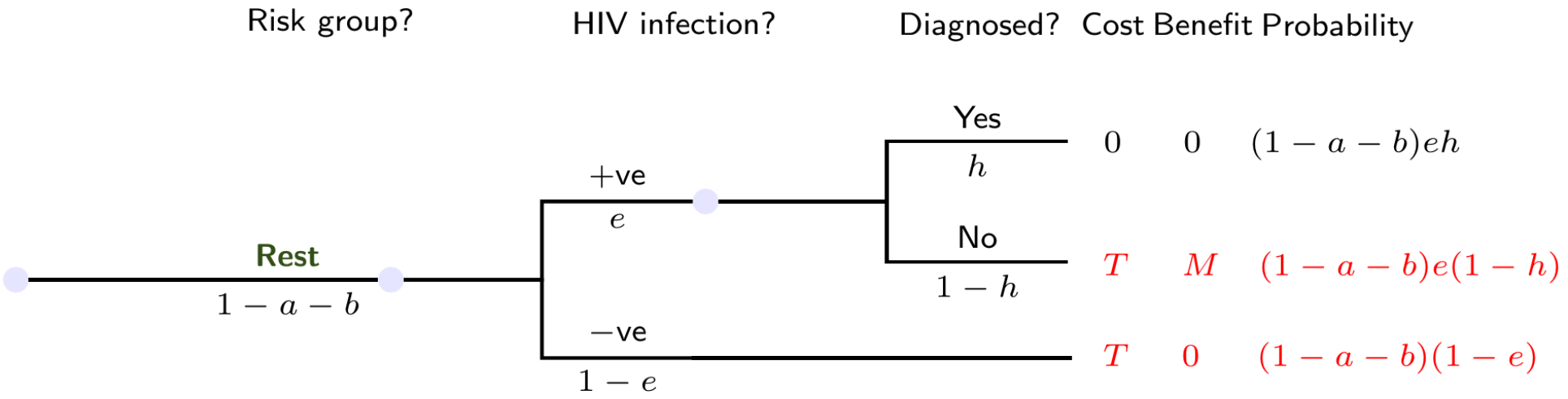
Ades et al (2002) Medical Decision Making

Targeted prenatal screening



SSA=Sub-Saharian Africans
IDU=Injecting Drug Users

Universal vs Targeted testing



$$\text{NB}(\boldsymbol{\theta}) = \begin{cases} 0 & t = 1, \text{targeted} \\ N(1-a-b)[e(1-h)(M-T) - T(1-e)] & t = 2, \text{universal} \end{cases}$$

- N = number of pregnancies per year
- $(1-a-b)$ = proportion of "Low Risk"
- M = net benefit of early maternal diagnosis
- e = HIV prevalence in "Low Risk"
- h = proportion of infected "Low Risk" already diagnosed
- T = cost of screening test (= £3)

Example – HIV screening decision model

Uncertainty in model inputs

$$\boldsymbol{\theta} = \begin{cases} N, M, T & \text{economic parameters} \\ a, b, e, h & \text{epidemiological parameters} \end{cases}$$

- N = 105,000
- T = £3
- M is uncertain
  - From previous model: M = 600,012 - 54, 296Y with $Y \sim$ Gamma$(0.56, 3)I(0, 2)$
- Epidemiology parameters estimated from multi-parameter evidence synthesis
  - Correlated
  - MCMC samples available

Example – HIV screening decision model

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Population EVPI

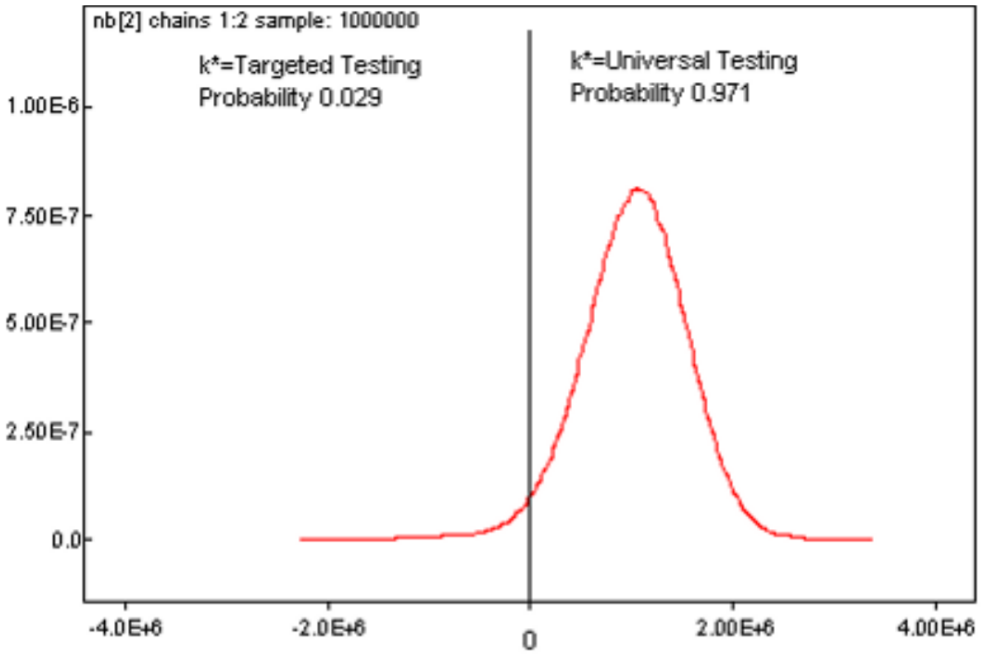
- NB is typically computed per individual patient
  - Need to multiple EVPI by the number of individuals expected to benefit per year
  - In HIV example population size included in NB, so already accounted for
- Also, expect the benefits of getting decision right to accrue for longer than 1 year
  - Until superseded...
  - In HIV example assume 10 year life span of screening format (discounted to give a 7.7217 multiplier)

Example – HIV screening decision model

R code: Cost effectiveness analysis for the HIV example

```
> # Read in 150,000 simulated values of M, a, b, e, h
> par <- read.table("hiv150.txt",header=TRUE)
> N <- 105000; T <- 3; Nsim <- nrow(par);
> Nt <- 2                                  # Nt=no. trts
>
> # Net Benefit based on current information
> NB <- matrix(rep(0,Nsim*Nt),Nsim,Nt)
> NB[,2] <- N*(1-par$a-par$b)*(par$M*par$e*(1-par$h) - T*(1-par$e*par$h))
> ENB <- apply(NB,2,mean)                  # Column means for each trt
> tstar <- which.max(ENB)                  # t* optimises ENB
>
> # Prob t* is cost-effective: checks if t=2 is optimal
> CE <- ifelse(NB[,2]>NB[,1],1,0)
> probCE <- mean(CE)                       # Prob t*=2 is cost-effective
>
> # Find maximum NB for each simulation (ie max across rows of NB)
> max.NBgain <- apply(NB,1,max) - NB[,tstar]
>
> # Compute EVPI
> EVPI <- 7.7217*mean(max.NBgain)
```

Results

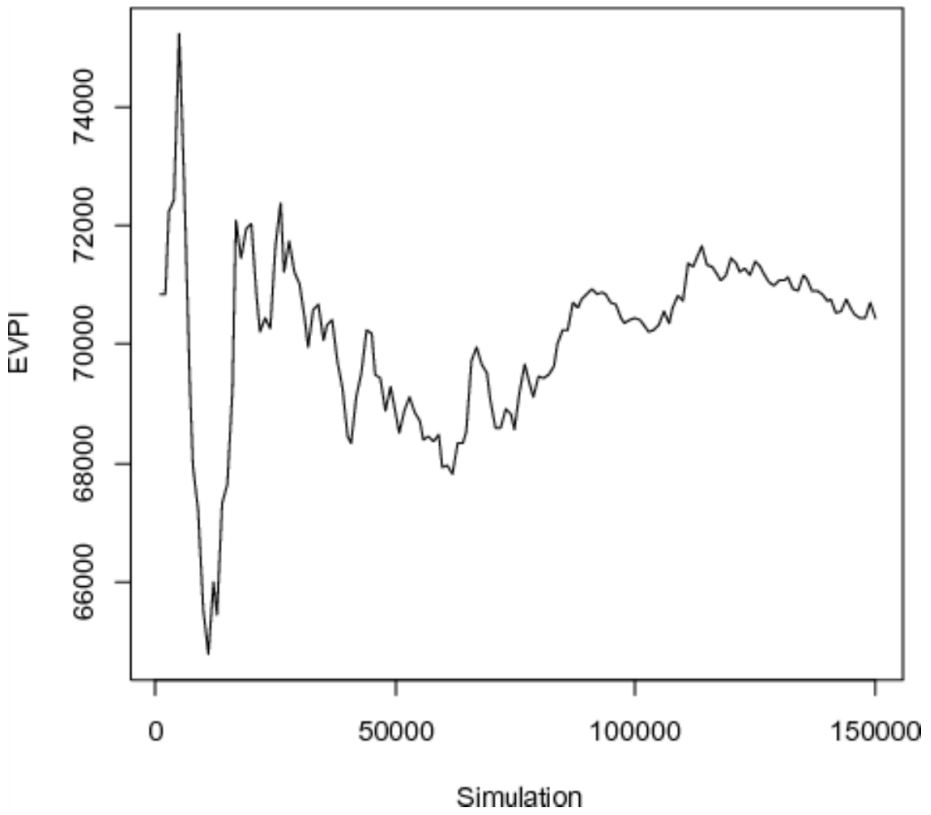


- $\mathrm{E}(\mathrm{IB}) =$ £1,023,931 Universal vs Targeted
- Optimal decision $t^* = 2$: Universal
- $\Pr(t^* = 2 \text{ is optimal}) = 0.971$
- EVPI = £71,670 per 10 years

Example – HIV screening decision model

R code: Check convergence

```
> # Running mean to assess convergence
> EVPI.run<-c(rep(0,150))
> for (i in 1:150) {
+  EVPI.run[i] <- 7.7217*mean(max.NBgain[1:(i*1000)])
+ }
>
>
> # Plot running mean of EVPI
> plot(seq(1000,150000,1000), EVPI.run, type="l",
+      lty=1,xlab="Simulation", ylab="EVPI")
```



Pilot Studies for NIHR and NICE

- Claxton et al (2004, 2005) conducted 2 pilot studies applying / integrating VOI to directly inform research priorities
  - NCCHTA (now NIHR NETSCC HTA) funds primary and secondary evaluative research
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Is further research required?

NO

- Physiotherapy for COPD or asthma in adults (EVPI = £0)

MAYBE

- Liquid based cytology (EVPI = £2.8m)
- AMD (EVPI = £25m)
- Children with asthma (EVPI = £15.7m)
- Recurrent UTI (EVPI = £4.6m)

YES, a priority for:

- Clopodogrel for stroke patients (EVPI = £865m): high prevalence
- NI for influenza (EVPI = £66.7m)
- Multiple sclerosis (EVPI = £86.2m)
- Glycoproteins (EVPI = £171m)

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Which subgroups?

Clopidogrel

- Research of most value for stroke and MI groups, but high value for all

AMD

- EVPI is higher for those with lower starting visual acuity score

UTI

- EVPI = £2.2m for non-infant girls with normal urinary tracts... but negligible for other risk groups (where low-dose anti-bacterial regimen is clearly cost-effective)

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Which comparators?

Multiple Sclerosis

- EVPI higher for RCT of glatiramer acetate (£14m) and interferonb-1b (£13.6m) than interferonb-1a (£7m)

UTIs

- EVPI is highest for 2 prophylactic regimens, rather than intermittent treatment, suggesting head-to-head trial

Asthma in children

- EVPI highest for 2 therapies, suggesting head-to-head trial

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Comments

- Research priorities cannot be based on efficacy alone
  - Asthma/COPD in adults had highest uncertainty in effect, but EVPI = £0
  - Clopidogrel and glycoproteins had substantial evidence on some outcomes, but large EVPI
- This analysis requires us to investigate further (see Lecture 12)

Next lecture