

Trial Based Economic Evaluation: Just Another Piece Of Evidence

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Is the purpose of evaluation to inform decisions?

- What are the decisions?
- What is required?
- Which evidence is relevant?
- Does uncertainty matter?
- What is the role of trials?
- Are there any dangers?

What decisions?

- Given existing evidence:
 - Which interventions/strategies should be implemented?
 - For which patient/population groups?
 - For what type of indications/settings?
- Is further evidence required to support decisions?
 - What type of evidence
 - What type of studies
 - For which patient groups
 - How much evidence
- Delay implementation until the evidence is available?

So what's required?

- Joint distribution of cost and outcomes
- For all alternative interventions/strategies
- Explore the full range of clinical policies
- For range of patient groups
- In the relevant decision context
- Over an appropriate time horizon

Should we consider all the evidence?

- Should social decision making consider all the evidence of relative effect?
 - Central tenant of EBM
 - Expected cost and outcomes
 - Characterisation of the uncertainty
- Should we compare all alternative interventions or only the selection included in a particular study?
- Should we also consider all the evidence for other parameters?
- Should we consider both direct and indirect evidence for all parameters?

Direct and indirect evidence?

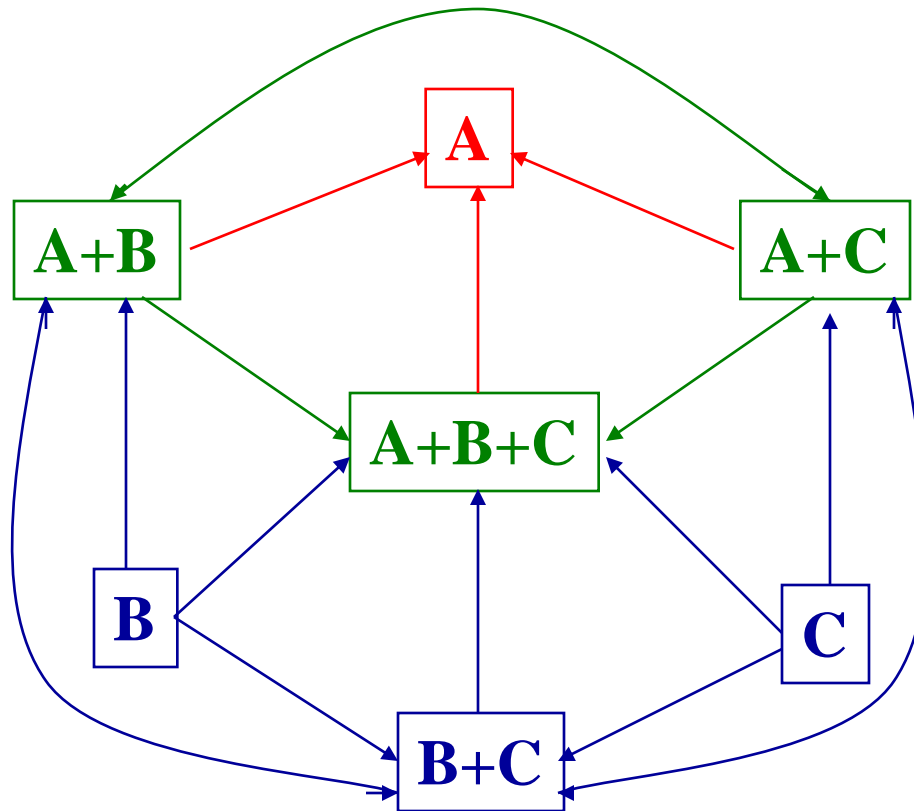
- Synthesis 1 and 2
- But compare all interventions?
 - Pair wise comparisons?
 - Use all the information
 - Estimate joint posterior LOR with correlations

RCTs

Alternative interventions

	A	B	C	D
1	x	x		
2	x	x		
3	x		x	
4	x			x
5		x	x	
6		x		x
7			x	x

Direct and indirect evidence?



- Estimates of parameter values
- Uncertainty surrounding estimates
- Correlations between parameters

Does decision uncertainty matter?

- Is an assessment of the consequences of decision uncertainty necessary for rational (expected value) decision making?
 - Is a characterisation of decision uncertainty a prerequisite for an assessment (formal or informal) of its consequences?
 - Does this require a synthesis of all evidence from a variety of sources?

Some examples from NICE

Implications for research prioritisation

Case Study	Patient Group	Population EVPI	EVPI for parameters
AMD Screening	Visual acuity 20/40 Visual acuity 20/80	£6.2m £15.3m	Quality of life with and without PDT (£3,370,000 for 20/40)
Glycoprotein IIb/IIIa	Acute treatment following non-ST-elevation acute coronary syndrome (scenario 2)	£171m	Relative risk of death for non acute PCI for GPA as medical management and for Clopidogrel (£85,041,000, and £68,137,000 respectively)
Clopidogrel and dipyridamole for secondary prevention	Stroke Transient Ischaemic Attack Myocardial Infarction Peripheral Arterial Disease (scenario 2)	£865m £250m £710m £240m	Relative risks of vascular and non vascular death (£780m for ASA-MR-dipridamole compared to clopidogrel in the stroke subgroup)
Neurominidase inhibitors	Otherwise healthy adults not at elevated risk of complications	£66.7m	Quality of life with influenza, the effect of oselatimivir and amantadine (£44.3m, £0.43m and £0.23m respectively)
Liquid Based Cytology	Women aged 18 to 64 years (scenario 3)	£20m	Specificity (£3.6m)
Disease modifying therapies for multiple sclerosis	Relapsing remitting and primary progressive multiple sclerosis (scenario 2)	£86.2m	Relative risk of progression for copaxone, Betaferon and rebif (22mg) (£14m, £13.6m and £7m respectively) Also the cost of care, costs of relapse and quality of life (£10m, £7m and £6m respectively)

Can any single study provide a basis for decision making?

- Should we adopt a technology?
- Is further evidence required?
- When would a trial be sufficient basis
 - Trial follow-up and time horizon identical
 - All relevant comparators included as arms
 - Patients and practice relevant to decision-making context
 - All parameters estimated
 - Only source of evidence for all parameters

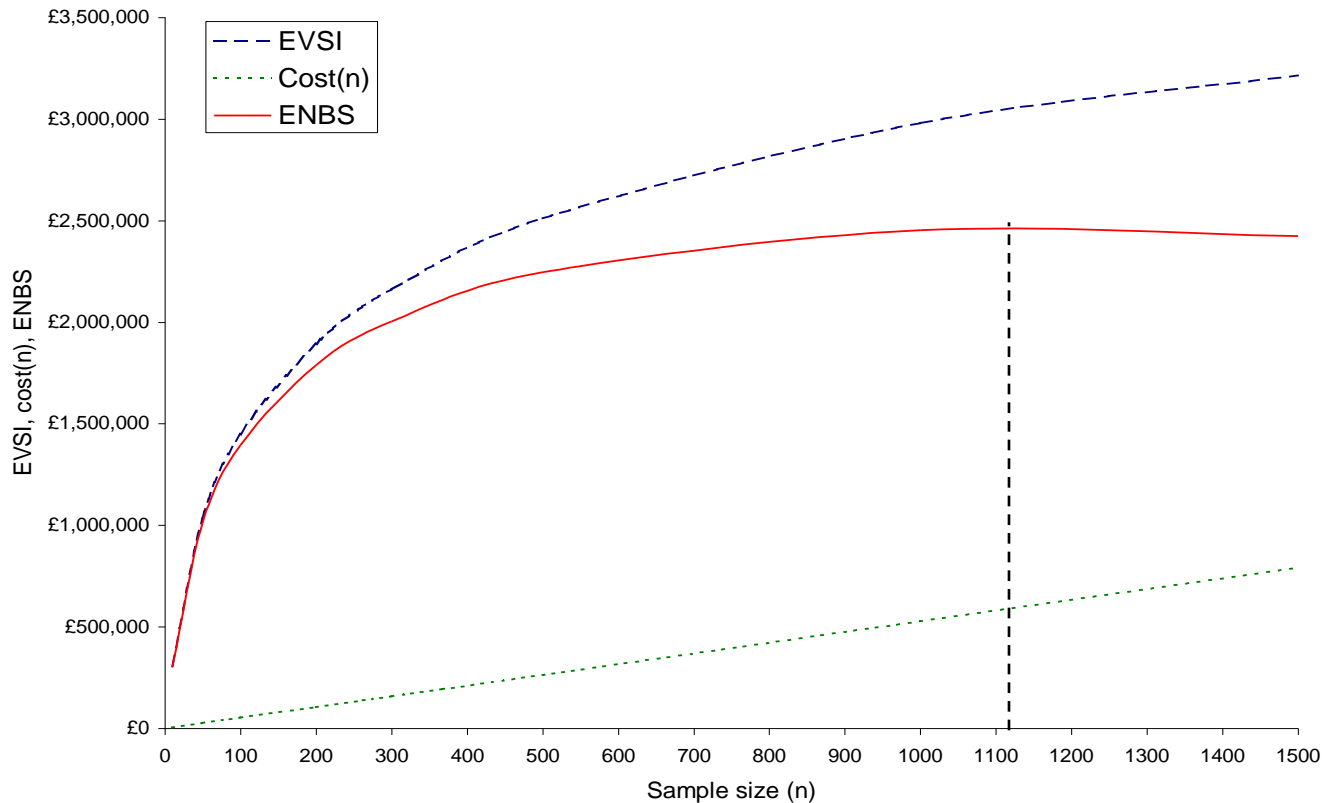
So what is the role of trials?

- As measurement
 - Particularly parameters subject to selection bias
 - Input to the synthesis of all evidence
- Implications for design
 - Useful for synthesis
 - Pragmatic trials (what is exchangeable)?
- Implications for reporting of evaluations
 - ICERs and certainly CEACs make little sense
 - Value of information without synthesis makes no sense

Do we need economic trials?

- Is Peto right? Its an empirical question

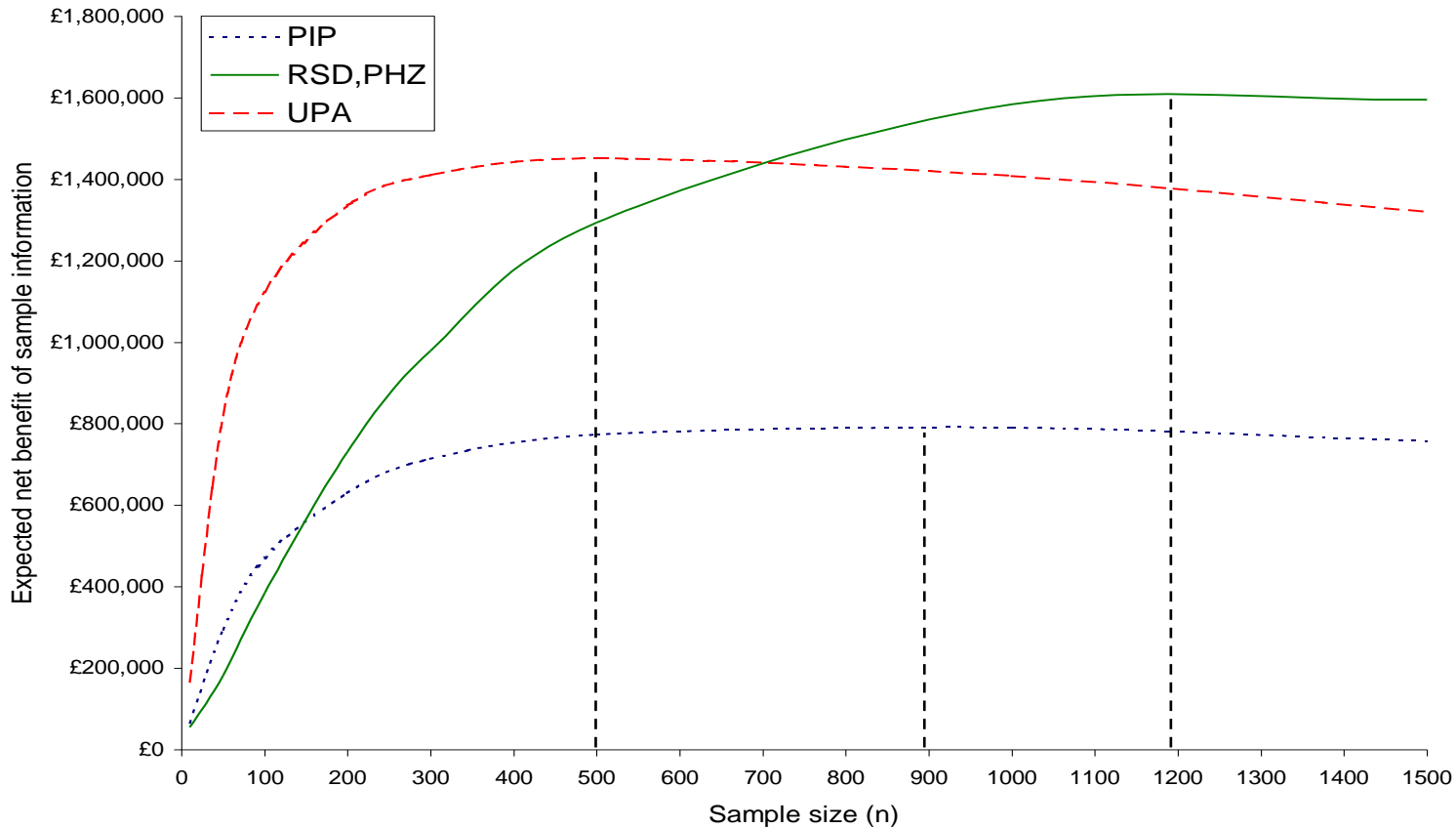
Value of a trial updating all parameters



Do we need economic trials?

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Value of a portfolio of studies



Why trial based evaluation?

- Historical dominance of frequentist analysis
 - Probability is the relative frequency of repeated events
 - Traditional Inferential rules
- Fully Bayesian decision theoretic analysis
 - Priors based on synthesis of accumulated evidence
 - Specification of the loss function (decision framework)

Leon Trotsky, Preface to The History of the Russian Revolution

- Entirely exceptional conditions, independent of the will of persons or parties, are necessary in order to tear off the fetters of conservatism and bring the masses to insurrection
- The masses go into revolution not with a preprepared plan of social reconstruction, but with a sharp feeling that they cannot endure the old regime

Leon Trotsky, Preface to The History of the Russian Revolution