Using economic modelling to contribute to the prioritisation and design and clinical trials: ready for prime time

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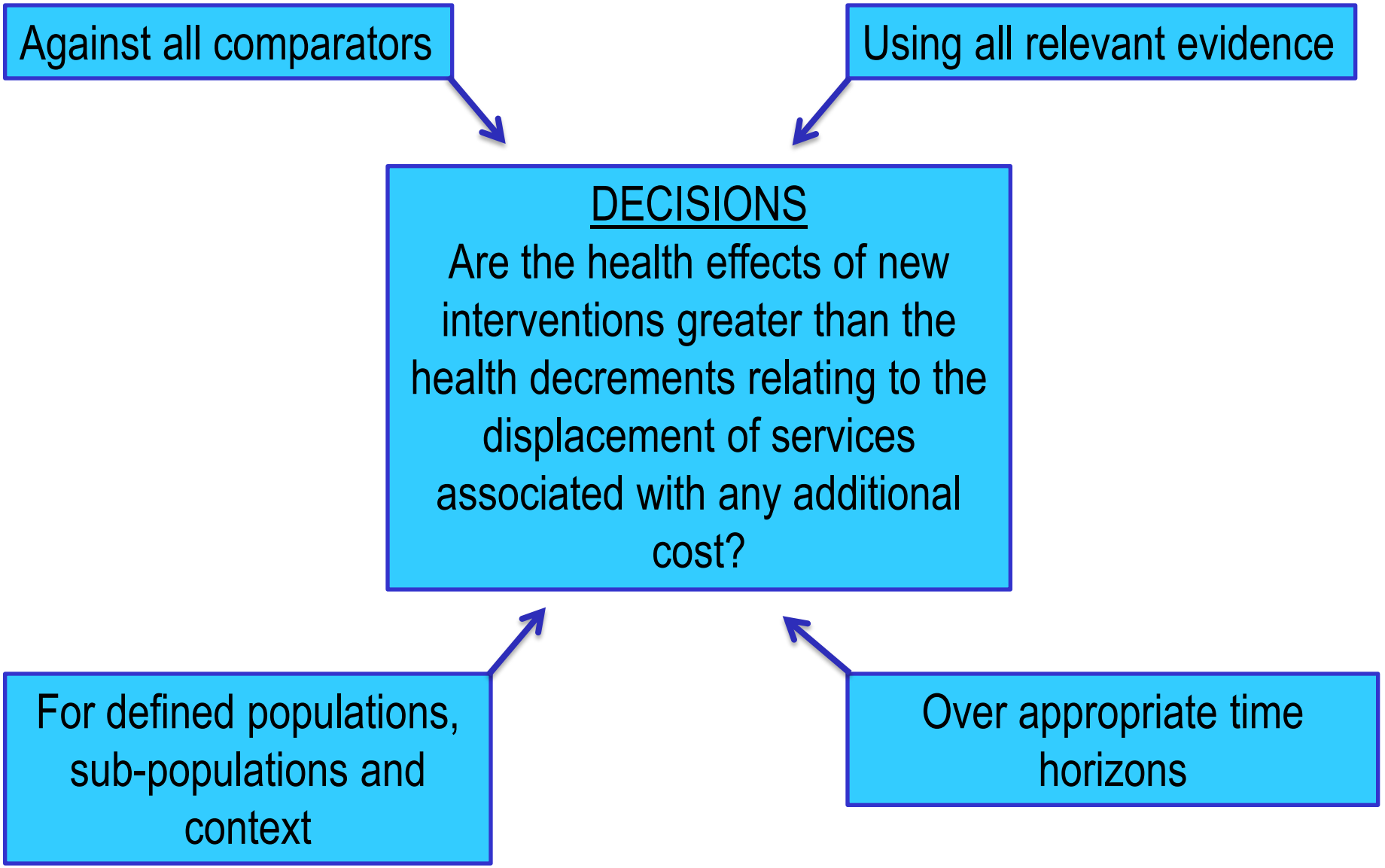
Overview

- The role of economic evaluation in supporting decisions
- What are the implications for how we prioritise and design evidence generation?
- Are economic methods being used to inform research funding?
- Expected value of information methods – the right tool?
- What other methods can help?

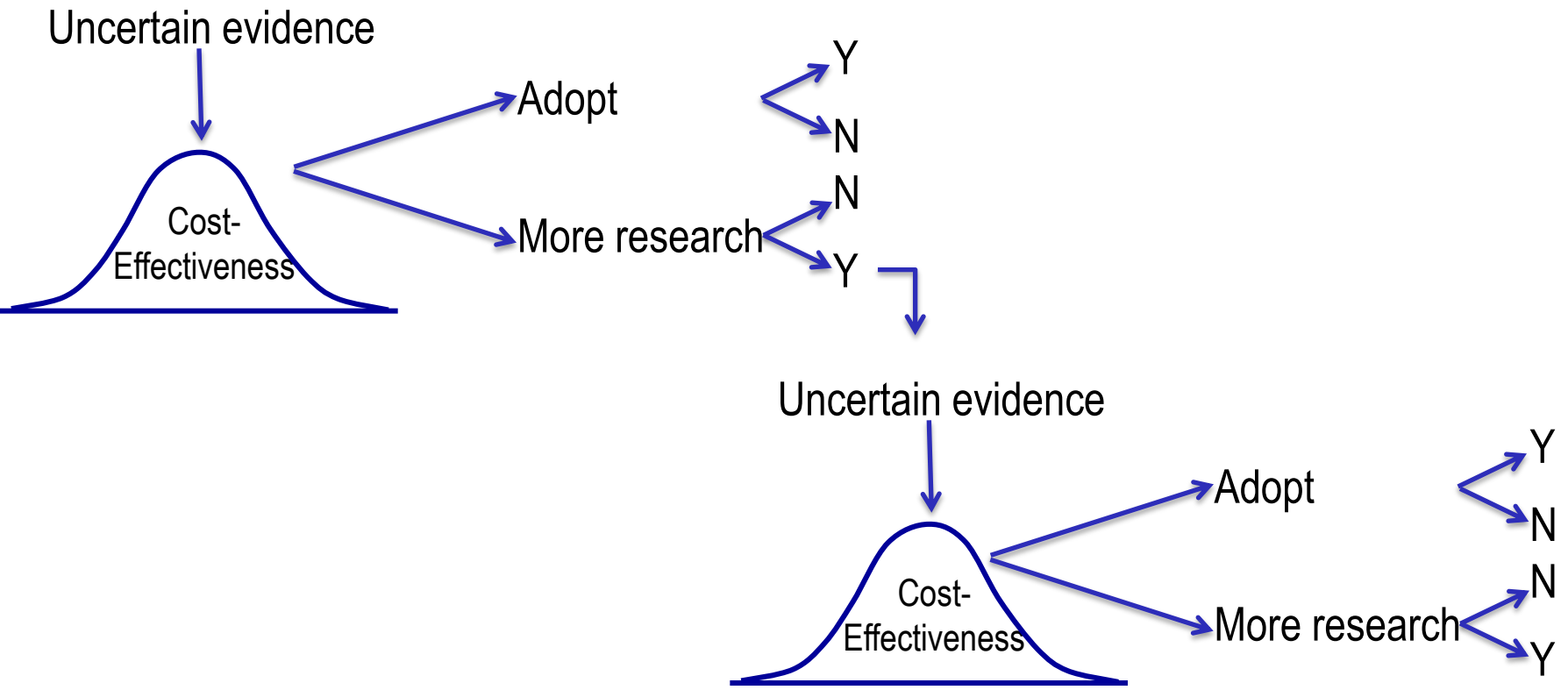
Context

- Growing role for economic evaluation, although prominence varies
- National vs. local impact of economic evaluation
- Policy impact likely to grow
  - Tighter budgets for health care
  - Pressure of transparency
- Continuous need to show value from R&D
- Timely to reflect on how economic evaluation is being used with trials

Role of economic evaluation



Iterative nature of evaluation



- Uncertainty cannot be eliminated
- Undertake research until its value < cost

Implications for new evidence generation

- Need to understand existing practice and evidence
  - All relevant existing evidence
  - Comparators
  - Role of new technology/intervention
  - Population and sub-groups
- Understand cost effectiveness of new intervention given existing evidence
- Understand uncertainty in cost-effectiveness (decision uncertainty)
- Determine priority research (and appropriate design) to reduce uncertainty in cost-effectiveness

How much of this is done?

• Systematic review of existing evidence	Usual
- New intervention	Usual
- Comparators	Rare
• Synthesis of existing clinical evidence	Sometimes
• Cost-effectiveness modelling	Very rare
• Inform trial design using economic modelling	Very rare

Some examples...

	EVAR	Reflux	RITA-3	MITRE
• Systematic review of existing evidence				
- New intervention	√	√	√	√
- Comparators	X	X	X	X
• Synthesis of existing clinical evidence	X	X	X	X
• Cost-effectiveness modelling	X	X	X	X
• Inform trial design using economic modelling	X	X	X	X

EVAR: Endovascular aneurysm repair. *Lancet* 2005; 365: 2179–86

REFLUX: Minimal access surgery compared with medical therapy in chronic reflux disease. *BMJ* 2008; 337;a2664

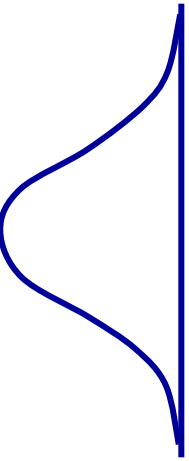
RITA-3: Interventioal versus conservative treatment for unstable angina or non-ST-elevation myocardial infarction. *Lancet 360: 743-751.*

MITRE: continuous glucose monitoring on HbA1c in insulin-treated diabetes. *Diabetic Medicine* DOI: 10.1111/j.1464-5491.2009

Do we have the tools to do it properly?

- What do we need?
  - Quantification of decision uncertainty
  - Quantification of costs of uncertainty
  - Cost of research
  - Marginal costs and benefits of specific studies
- Expected value of information (EVI)
  - Expected value of perfect information
  - Expected value of sample information
- Increasing number of examples in published literature
- Often requested as part of HTA Programme secondary research

Calculating EVPI



	Treatment A	Treatment B	Optimal choice	Maximum Net benefit	Opportunity Loss
Iteration 1	9	12	B	12	0
Iteration 2	12	10	A	12	2
Iteration 3	14	20	B	20	0
Iteration 4	11	10	A	11	1
Iteration 5	14	13	A	14	1
Expectation	**12**	**13**		**13.8**	**0.8**

Current information = 13
Perfect information = 13.8
EVPI = 13.8 - 13 = 0.8

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

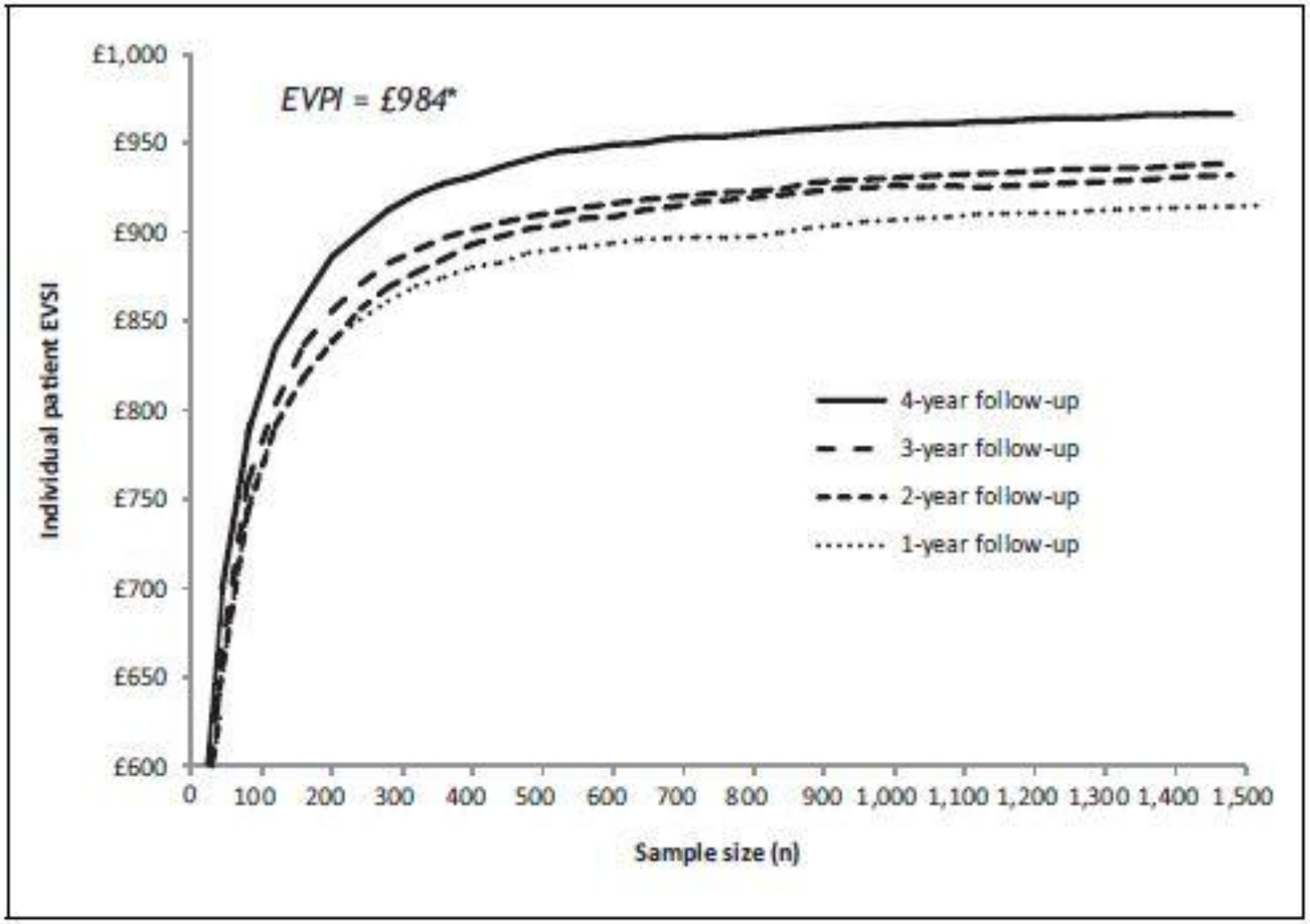
Examples of EVI having impact

Table 3 | Interventions in each maternal risk group with a probability of being cost effective of at least 1%*

Maternal risk groups in hierarchical order	% of total population	Intervention	Probability of being cost effective	Expected value of information per year in UK
Preterm deliveries (<37 weeks)				
1. Planned caesarean section	0.80	IV antibiotic	0.5870	£5 281 333
		Oral antibiotic	0.4120	
2. Previous baby with GBS	0.01	IV antibiotic	0.8590	£7 820
		Oral antibiotic	0.1370	
3. Positive urine or vaginal swab for GBS in current pregnancy	0.44	IV antibiotic	0.9730	£81 600
		Oral antibiotic	0.0178	
4. Fever ≥38.0°C in labour	0.25	IV antibiotic	0.7800	£539 467
		Oral antibiotic	0.2160	
5. Rupture of membranes before onset of labour	2.41	IV antibiotic	0.5800	£12 806 667
		Oral antibiotic	0.4190	
6. Spontaneous labour (membrane rupture <2 hours before or after onset of labour)	3.43	IV antibiotic	0.8590	£4 193 333
		Oral antibiotic	0.1370	
Term deliveries (≥37 weeks)				
7. Planned caesarean section	7.99	Oral antibiotic	0.6720	£1 586 667
		IV antibiotic	0.3270	
8. Previous baby with GBS	0.08	IV antibiotic	0.6060	£30 600
		Oral antibiotic	0.3930	

Colbourn *et al. BMJ* 2007;335;655

Fewer examples of expected value of sample information - EECP



McKenna and Claxton. *Medical Decision Making*, in press, DOI: 10.1177/0272989X11399921

Routine use of EVI methods

New methods of analysing cost effectiveness

Value of information analyses must be integrated into the process of commissioning primary research

RESEARCH, p 655

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Interest in whether health interventions are value for money as well as effective has meant that the term cost effectiveness[1] is commonly used (and sometimes misused) in the clinical literature. Consequently, methods for determining cost effectiveness have been refined, especially techniques for synthesising evidence and representing uncertainty in the results of such evaluations. Techniques such as multiparameter evidence synthesis[2] and value of information analysis[3] are now routinely integrated into cost effectiveness studies, especially health technology

This contrasts with the Cochrane review approach, which typically uses only randomised evidence to assess a single treatment comparison.

In addition, a probabilistic analysis of uncertainty in the parameters of the model allows a full assessment of the implication of the estimated uncertainty for the decision. This means the analysis can answer two fundamental questions relating to the choice between the strategies evaluated. Firstly, on the basis of the existing evidence, what is the preferred course of action? Secondly, should additional information

Briggs. BMJ 2007;335:622-3

Why is EVI not getting used to guide research funding decisions?

- Limited use of EVI by research funders/ commissioners
  - 2003 pilot work by HTA Programme*
  - Little experience with key concepts
  - No scope to interact with the modelling
  - Challenge of making it practical
- Limited use in trial proposals
  - How many health economists understand and use EVI?
  - Challenge of communication and training
  - How influential are economists in developing proposals
  - Does modelling and EVI need additional funding?

* Claxton *et al*. *Health Technology Assessment* 2004; Vol. 8: No. 31
Claxton and Sculpher. *Pharmacoeconomics* 2006; 24 (11): 1055-1068

Are there alternatives to EVI?

- Currently little economic analysis is used to help commissioners prioritise research or assess designs
- Conventional power calculations available for economics
  - Inconsistent with the needs of decision makers
  - Not used!
- Contextual information about prioritisation: decision uncertainty rather than burden of illness
- Resource allocation issues not always a priority
- Are trial endpoints relevant to resource allocation decisions?
- Would the minimum ‘detectable’ effect size result in cost-effectiveness?

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