Cost-Effectiveness Analysis for (NICE) Decision Making New Guidelines and Future Challenges

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Starting points

- Increasing use of cost-effectiveness analysis to inform real decisions in health care
- What does this imply for analytical methods?
- Recent NICE methods guidance born out of these considerations
- Some major methods challenges to be addressed

Outline

- Requirements for decision making
- The NICE Reference Case
- Methods challenges
  - Evidence synthesis
  - Opportunity cost
  - Setting research priorities

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Two decisions for new health care technologies

Is the technology cost-effective based on existing evidence?

Is additional research cost-effective?	Yes	No
Yes	Adopt Demand additional evidence Revisit decision	Do not adopt Demand additional evidence Revisit decision
No	Adopt Do not demand extra evidence Review decision if other evidence emerges	Do not adopt Do not demand extra evidence Review decision if other evidence emerges

Analytical requirements for decision making

Adoption decision

Defining the decision problem

- Compare all feasible alternative interventions/strategies
- Explore the full range of clinical policies
- For range of patient sub-groups

Analytical requirements for decision making

Adoption decision

Clear objective function

- What is the decision-maker trying to maximise?
- Strong argument for some measure of health benefit
- Most decisions (all?) require generic measure of health (e.g. QALY)
  - Comparability within an evaluation (e.g. efficacy vs adverse events)
  - Comparability between decisions
  - Facilitates comparison with opportunity costs

Analytical requirements for decision making

Adoption decision

Defining the constraints

- Range of constraints in a decision
- Most obviously, a budget constraint
  - Strong normative arguments for societal perspective
  - Particular decision-makers may have narrower budget constraint (potential inefficiencies)
  - Need for consistency between decisions
  - Should quantify opportunity costs explicitly
- Should be defining and using other constraints, e.g.
  - Capacity
  - Equity

Analytical requirements for decision making

Adoption decision

Incorporation of all relevant evidence

- Need to estimate large number of parameters:
  - Baseline effects (natural history)
  - Treatment effects (intended and unintended)
  - Quality of life
  - Resource use
  - Costs
- Need to identify all sources systematically
- Synthesise the evidence allowing for:
  - Different designs
  - Precision
  - Varying quality
  - Heterogeneity

Analytical requirements for decision making

Research decision

Explicit quantification of uncertainty in adoption decision

- Uncertain about every parameter in an analysis
- Need to combine uncertainty for all parameters
- Express in terms of decision uncertainty: what is the probability the correct decision is being made?

Analytical requirements for decision making

Research decision

Quantification of the cost of making the wrong decision

- A wrong decision will have ‘costs’
  - Resources wasted
  - Health gains forgone
- Expected cost of uncertainty:

  Probability of making a wrong decision X

  cost of making wrong decision

Analytical requirements for decision making

Research decision

What is the value of additional research?

- Expected cost of uncertainty = expected value of perfect information (EVPI)
- If cost of research is less than EVPI, research is potentially efficient
- Will need to identify most efficient research design

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The concept of the Reference Case

- Concept introduced by Washington Panel
- Range of uncertainties in (economic) evaluation methods – values and technical
- But need for consistency in approach for decision making
- Reference case defines the methods which should be used *in one particular analysis*
- Does not preclude other *additional* analyses

Summary of Reference Case requirements (1)

Element	Reference case
Defining the decision problem	Consistent with NICE's scope
Perspective on costs	NHS and PSS
Perspective on outcomes	All health effects on individuals
Type of study	Cost-effectiveness analysis

Summary of Reference Case requirements (2)

Element	Reference case
Synthesis of outcome evidence	Systematic review
Measure of health benefits	QALYs
Health state descriptions	Validated generic measure
Method of preference elicitation	Choice-based

Summary of Reference Case requirements (3)

Element	Reference case
Source of preference data	Sample of public
Discount rate	Annual rate of 3.5% on costs and health effects
Equity	QALY given the same weight for all recipients
Dealing with parameter uncertainty	Probabilistic sensitivity analysis

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Challenge of evidence synthesis

Mixed treatment comparisons (1)

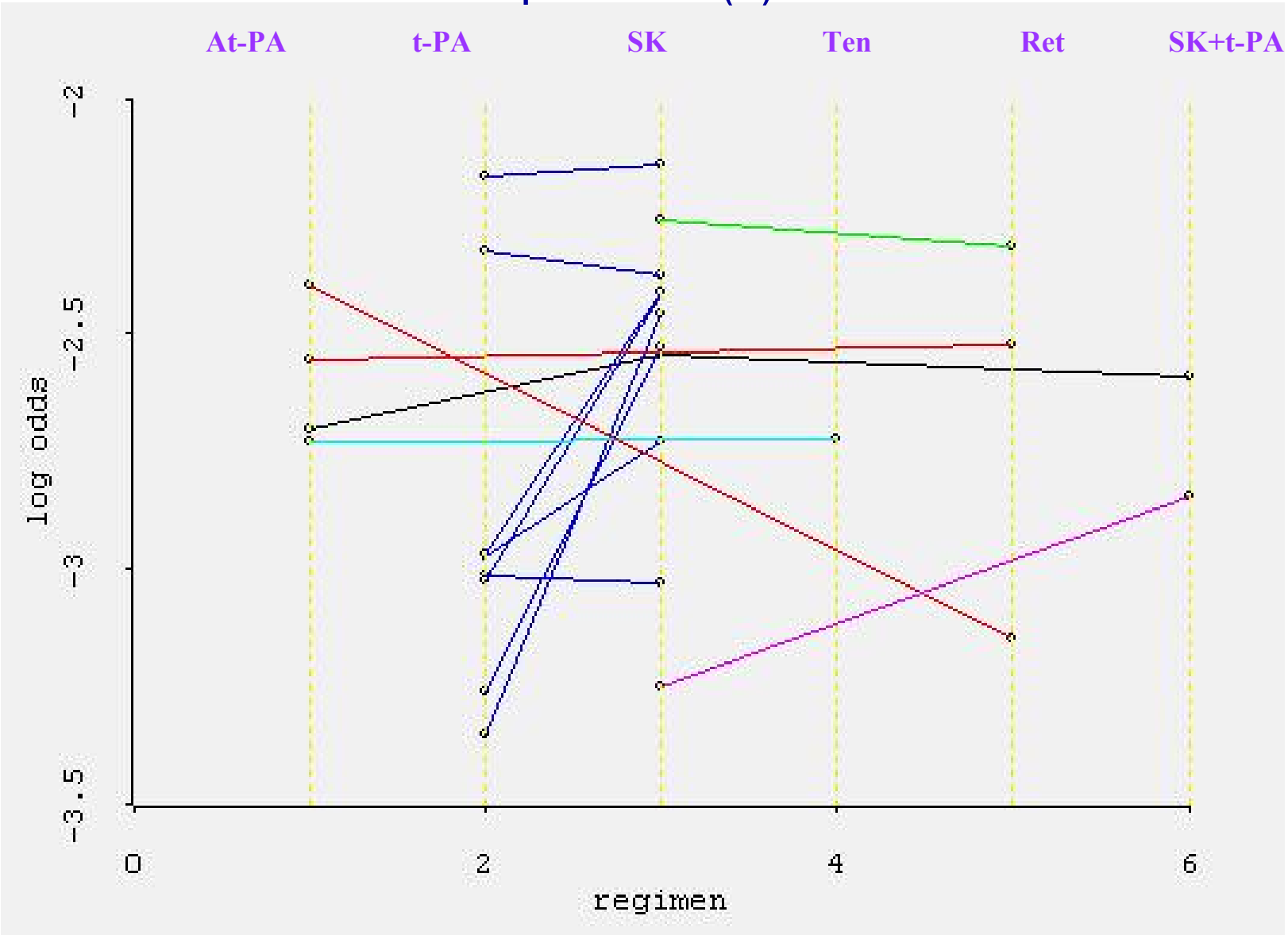
Thrombolytic drugs post AMI

Number of RCTs	SK	t-PA	acc t-PA	t-PA +SK	r-PA	TNK
1	X		X	X		
8	X	X				
1	X			X		
1			X			X
2			X		X	
1	X				X	

- Mixed treatment comparisons
- 14 RCTs
- 6 treatments

Challenge of evidence synthesis

Mixed treatment comparisons (2)



Bayesian hierarchical models

Building chains of evidence

Number of RCTs	SK	t-PA	acc t-PA	t-PA +SK	r-PA	TNK
1	X		X	X		
8	X	X				
1	X			X		
1			X			X
2			X		X	
1	X				X	

TNK vs SK No

TNK vs accTPA Yes

accTPA vs SK Yes

Challenge of evidence synthesis

Bayesian hierarchical models

	Pr("least mortality")		Mortality %	
	Fixed	Random	Fixed	Random
SK	0.00	0.00	6.5	6.6
t-PA	0.00	0.11	6.4	6.3
acc t-PA	0.41	0.24	5.7	5.9
SK + t-PA	0.01	0.09	6.3	6.5
ten	0.41	0.35	5.7	6.0
ret	0.16	0.21	6.9	6.0

Other challenges in evidence synthesis

Outcome measures – example of epilepsy

Study	Duration (weeks)	Treatment	Response		Treatment	Response	
			Complete	Partial		Complete	Partial
1	12	Placebo	-	8%	TGB		26%
2	16	Placebo	…	…	TGB	…	…
3	12	Placebo		14%	LTG		33%
4	14	Placebo		11%	LEV		40%
5	12	Placebo	1%	10%	LEV	10%	32%
6	12	Placebo	1%	14%	LEV	8%	39%
7	24	Placebo		12	OXC		50%
8	12	Placebo	2	24	TPM	6%	45%
9	14	Placebo		13	TPM		48%
10	11	Placebo	0	8	TPM	9%	35%
11	16	Placebo	0	18	TPM	4%	47%

Other challenges in evidence synthesis

Also with utilities…

	Clinical	D-S QoL	Utility
Study 1	✓		
Study 2	✓	✓	
Study 3		✓	✓
Study 4	✓	✓	✓
Study 5	✓		
Study 6	✓		✓

Other challenges in evidence synthesis

Follow-up periods

	30 day	6 month	1 year
Study 1	✓		
Study 2	✓	✓	
Study 3		✓	✓
Study 4	✓	✓	✓
Study 5	✓		
Study 6	✓		✓

Other challenges in evidence synthesis

Intermediate end points

		Intermediate endpoint	Final endpoint
Study 1	A vs B	✓	
Study 2	A vs C	✓	✓
Study 3	B vs D	✓	✓
Study 4	A vs B	✓	
Study 5	A vs E	✓	✓
Study 6	C vs E	✓	

Being explicit about opportunity cost

The myth of the lamda

- The ‘maximum acceptable ICER’ now embedded in cost-effectiveness analysis
- Use of a ‘rule of thumb’ is always arbitrary and hidden opportunity cost
- Appropriate use of CEA requires explicit quantification of opportunity cost resulting from budget constraint
- Health gains lost from displaced programme(s)
- Need formal framework for quantification of opportunity cost

A more formal framework for constrained optimisation

- Use of mathematical programming to maximise objective function subject to budget constraint
- Shadow price of budget constraint is the ‘correct’ threshold
- Other constraints can be formally expressed:
  - Resource
  - Equity
  - ‘Political’
- Major challenges:
  - Evidence
  - Uncertainty
  - Local variation

Setting research priorities

- Value of information methods available to inform research priority setting
- Policy challenge: joined up decision-making regarding adoption and research priorities
- Methods challenges:
  - Handling correlations (e.g. MTC)
  - Computational burden of value of sample information methods

Other methods challenges

- Defining an appropriate objective function:
  - Consistent generic measure of health
  - Adding non-health attributes
  - Reflecting equity considerations in the objective function
- The challenges of modelling
  - Identifying all evidence
  - Handling structural uncertainty
- Implementation issues

Conclusions

- Formal use of CEA to make decisions focuses the mind!
- There is a gap between much applied CEA and the needs of decision making
- Need clarity about analytical requirements
- Presents a series of methodological questions