An Introduction to Economic Evaluation Methods

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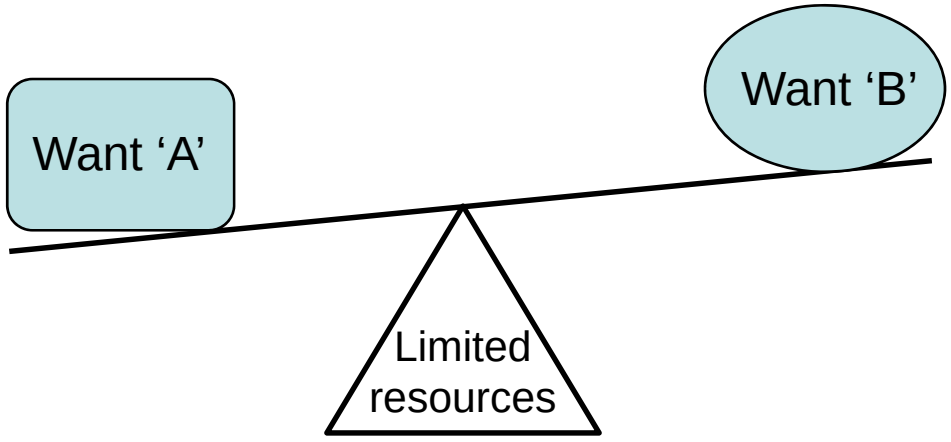
Overview

- Key economic concepts
- Economic evaluations
- Steps required to undertake an economic evaluation
- Critical appraisal of economic evaluations
- Essential ingredients of an economic evaluation (costs and health outcomes)
- Incremental cost-effectiveness ratio (ICER)
- Threshold of cost-effectiveness
- Decision-making process,
  National Institute for Health and Care Excellence (NICE)

Economics……

Economic evaluation is consistent with the fundamental principles of economics:

- Limited resources
- Unlimited ‘wants’
- Choices need to be made between alternative uses of resources



Choose between which ‘wants’ we can ‘afford’ given our resource budget constraint

Two fundamental concepts.....

Concept 1: Opportunity cost

The cost of an alternative use of resources that must be forgone in order to pursue a certain action. Put another way, the benefits you could have received by taking an alternative action

E.g. The opportunity cost of going to college is the money you would have earned if you worked instead

In healthcare, the opportunity cost of a particular deployment of resources is the displacement of health elsewhere

Cost-effectiveness analysis

Opportunity cost

Within a fixed budget constraint, if the healthcare system spends more on one thing, it has to do less of something else

You can only spend £1 once

The ‘opportunity cost’ is the value of the next best alternative use of resources

Source: Peter Littlejohns, The Challenge of Health Care in Europe: “value for money”

Two fundamental concepts.....

Concept 2: Efficiency

The use of resources so as to maximise the production of goods and services. Every resource is optimally allocated in the best way while minimising waste and inefficiency

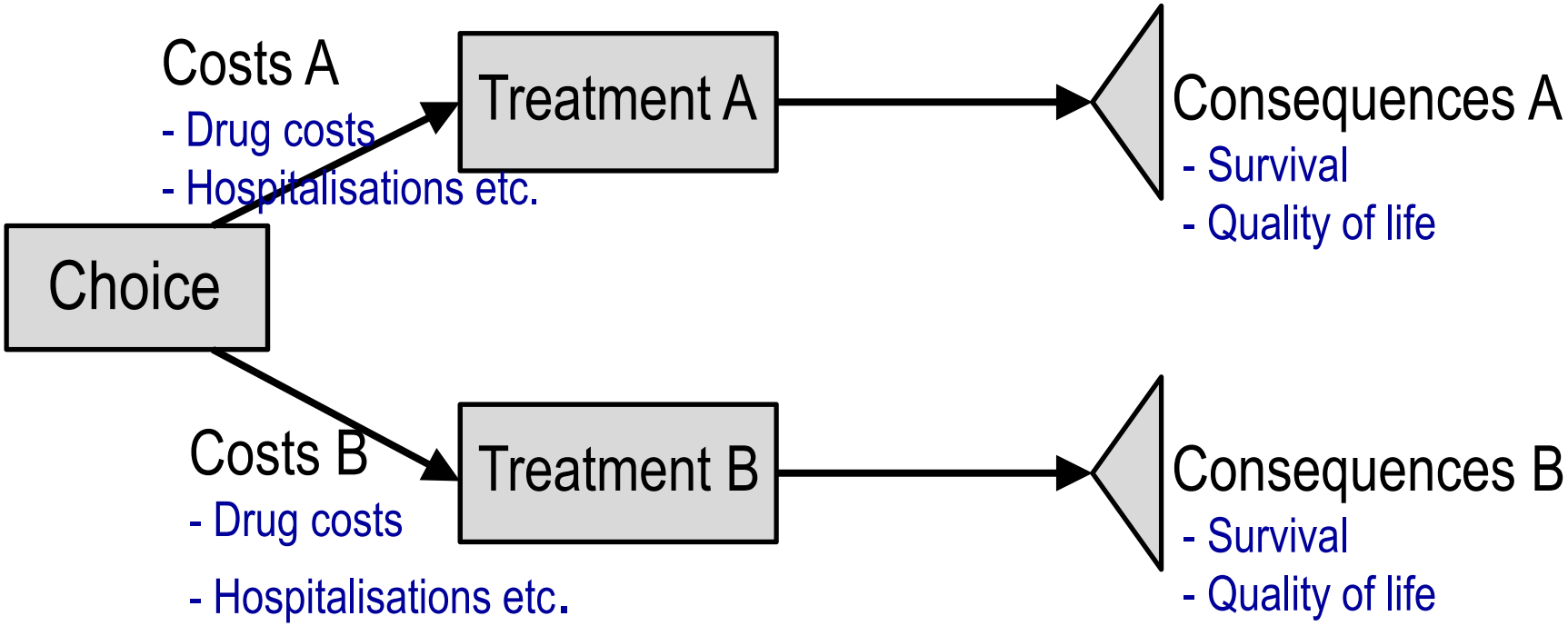
In healthcare, the decision maker's objective is to ensure that a particular healthcare programme represents an efficient use of resources

Choose programmes which maximise total health benefits subject to the budget constraint (resource constraints)

Economic evaluation

Definition of economic evaluation:

"the comparative analysis of alternative courses of action in terms of both their costs and their consequences"



Economic evaluation

The basic task of an economic evaluation

Identify → Measure → Value → Compare

the costs and consequences of the alternatives being considered

Incremental benefits	Incremental costs: +	0	−
+	?	✓	✓
0	X	-	✓
−	X	X	?

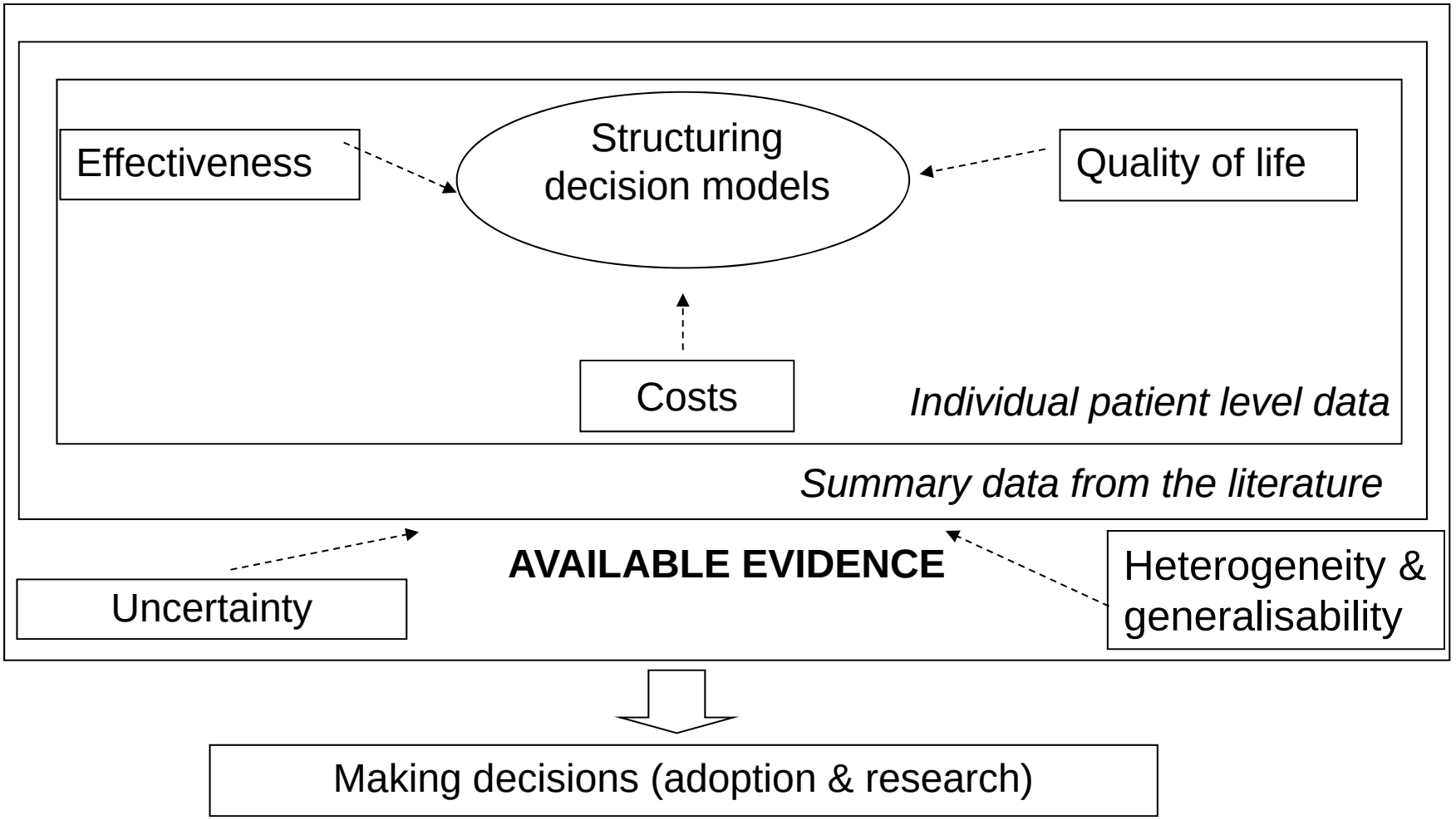
Types of economic evaluation

Type of analysis	Measurement of costs	Identification of consequences	Valuation
Cost-minimisation	Monetary units	- None - Identical in all respects	Least cost alternative
Cost-effectiveness	Monetary units	- Single outcome - Common effect - Natural units, e.g. blood pressure reduction	Cost per unit of outcome in natural units
Cost-utility	Monetary units	- Single or multiple effects - Not necessarily common - Valued in utility, e.g. QALYs	Cost per unit of outcome, e.g. QALY
Cost-benefit	Monetary units	- Same as CUA but valued in monetary values	Net monetary units

Steps of an economic evaluation

1. Define the economic question and the perspective of the study
2. Define the alternative treatments to be evaluated
3. Determine the study design
4. Identify, measure and value the costs of the treatment and the alternative treatments
5. Identify, measure and value the benefits of the treatment and the alternative treatments
6. Adjust costs and benefits for differential timing
7. Measure the differential costs and benefits of the treatments
8. Analyse the incremental estimates
9. Test the sensitivity of the results
10. Assess the generalisibility and limitations of the study

Structure of an economic evaluation



Critical appraisal: The 10 commandments

- Checklist for the critical appraisal of economic evaluations
- First published in Drummond *et al* (1987) *Methods for the Economic Evaluation of Health Care Programmes*, Oxford University Press.

- Studies with poor methodology can be misleading
- Those bidding for more resources often claim that the therapy concerned is ‘cost-effective’
- Published studies are often cited in support of such claims

Critical appraisal: The 10 commandments

1. Was a well-defined question posed in answerable form?
2. Was a comprehensive description of alternatives given?
3. Was there evidence that effectiveness had been established?
4. Were all the important and relevant costs and consequences for each alternative identified?
5. Were costs and consequences measured accurately/appropriately?
6. Were costs and consequences valued credibly?
7. Were costs and consequences adjusted for differential timing?
8. Was an incremental analysis performed?
9. Was allowance made for uncertainty?
10. Did presentation/discussion of results include all issues of concern?

1. WAS A WELL-DEFINED QUESTION POSED IN AN ANSWERABLE FORM?

- Does the study examine both costs and consequences of each alternative?
- Does the study compare competing alternatives (should be identified & justified)?
- Does the study state the viewpoint (perspective) taken?

Importance of the viewpoint (perspective)

- Different perspectives:
  - Government/NHS
  - Healthcare institutions, e.g. hospital
  - Third party payers (insurance company)
  - Patient and family
  - Societal

- The perspective will determine which costs and consequences to identify, measure and value

- Budget constraint

2. WAS A COMPREHENSIVE DESCRIPTION OF THE COMPETING ALTERNATIVES GIVEN?

- What are the relevant alternatives?
- Need to know whether the options apply in your setting (i.e. availability of equipment or facilities)
- Were any relevant alternatives omitted?
- Was (should) a ‘do-nothing’ alternative (be) considered?

3. WAS THE EFFECTIVENESS OF THE PROGRAMMES OR SERVICES ESTABLISHED?

- Hierarchy of evidence:

  randomised controlled trials (RCTs) > case controlled studies > observational clinical series

- Was a systematic review of clinical evidence used?

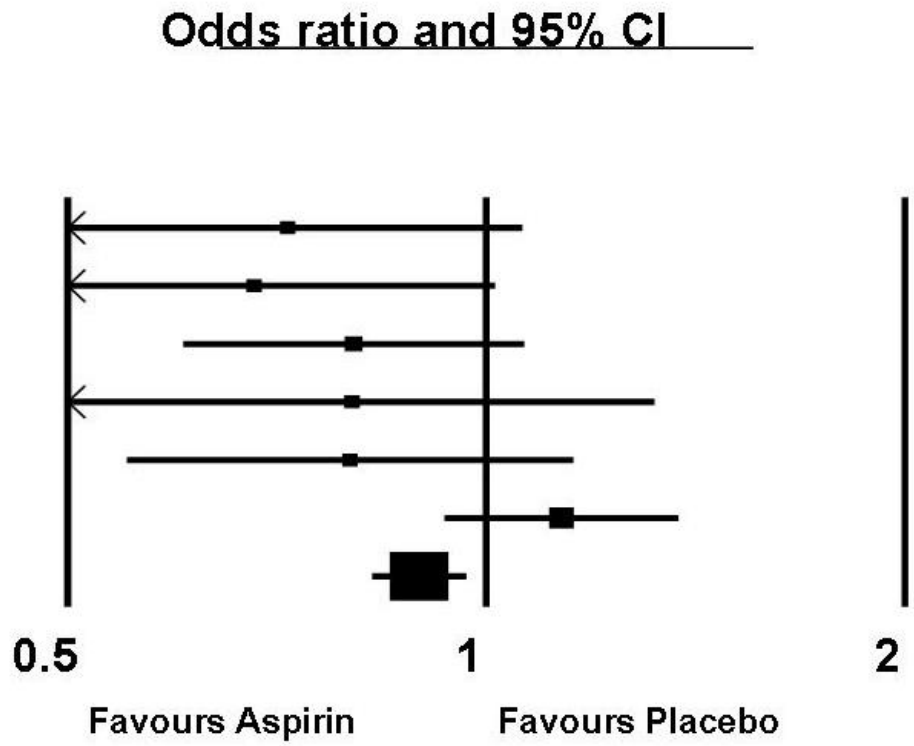
- Were observational data used? Were the potential biases identified?

- What was the measure of treatment effectiveness?

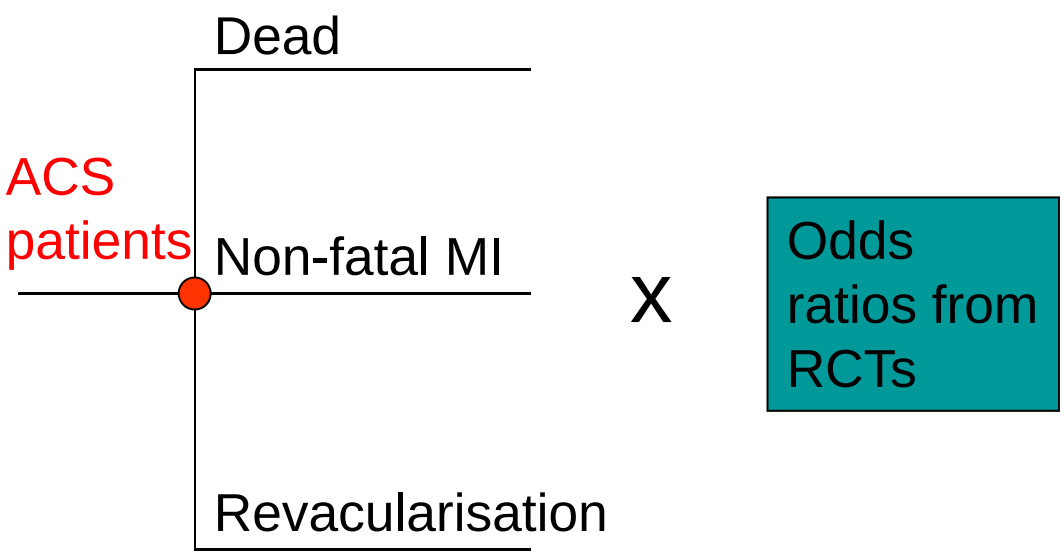
Evidence synthesis

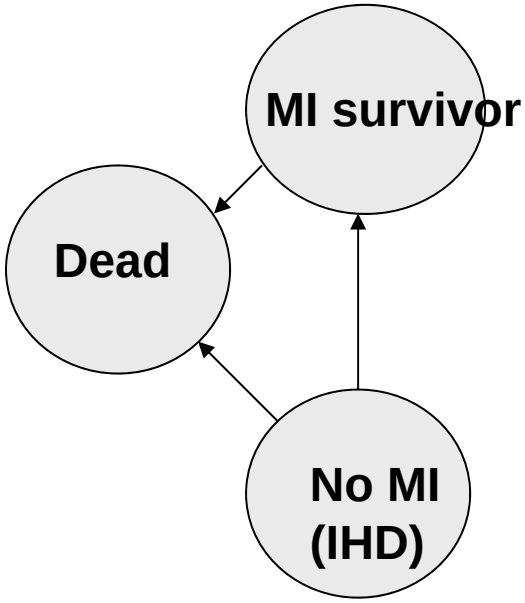
- Systematic review to identify all relevant evidence
- Meta-analysis to synthesise the evidence
- Mixed treatment comparisons
- Survival analysis

Study name	Odds ratio	Lower limit	Upper limit
MRC-1	0.72	0.49	1.06
CDP	0.68	0.46	1.01
MRC-2	0.80	0.61	1.06
GASP	0.80	0.49	1.32
PARIS	0.80	0.55	1.15
AMIS	1.13	0.93	1.37
ISIS-2	0.89	0.83	0.97



Application of Glycoprotein IIb/IIIa antagonists in acute coronary syndrome





Part 1: Baseline event rates
- Data from PRAIS-UK (n=1046) and Leeds (n=112)
- Costs of drugs, hospitalisation and procedures

Part 2: GPA effects
- Data from meta-analysis of RCTs

Part 3: lifetime extrapolation
- Data from Nottingham Heart Attack Register (n=1279)
- Costs of hospitalisation and procedures

Source: Palmer *et al. International Journal of Cardiology* 2005;100:229-240.

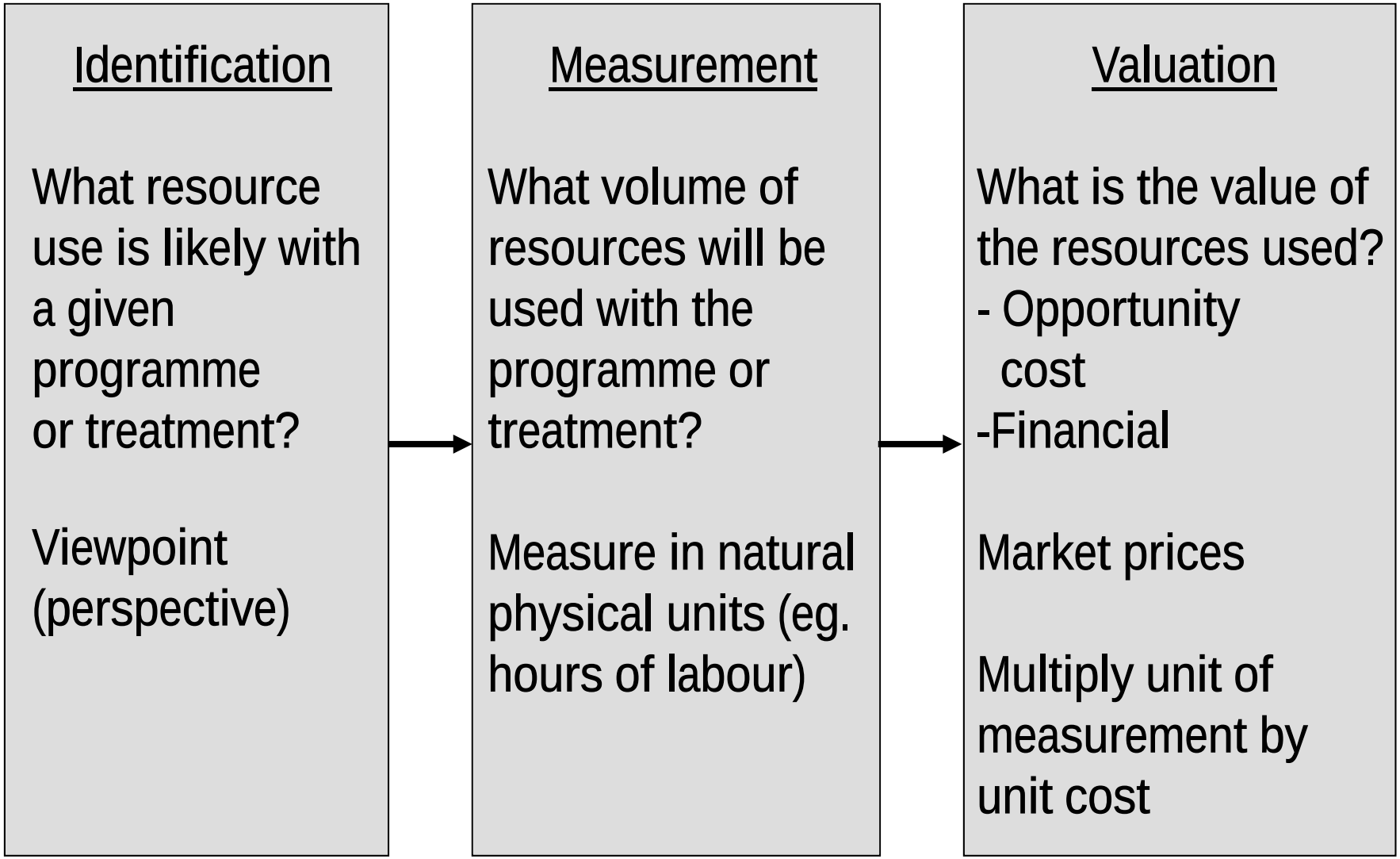
4. WERE ALL IMPORTANT AND RELEVANT COSTS AND CONSEQUENCES FOR EACH ALTERNATIVE IDENTIFIED?

- Depends on the viewpoint (perspective) of study

5. WERE COSTS AND CONSEQUENCES MEASURED ACCURATELY IN APPROPRIATE PHYSICAL UNITS?

6. WERE COSTS AND CONSEQUENCES VALUED CREDIBLY?

Resources and costs



Resources and costs

Direct costs

Health services resource use
- inpatient stay,
- outpatient visits,
- tests,
- drugs
- GP, nurse, consultant time
- equipment space/facilities

Usually categorised as:
- capital costs
- overheads
- labour
- consumables

Indirect costs

Wider costs to society
- productivity losses
- Measured by human capital approach, friction cost method

Patient and family costs
-Out of pocket expenses

'Give it to me straight, doc, how long will my car have to spend in the hospital car park?'

Sources of unit costs

- Published sources
  - Government (UK NHS reference costs)

    Payment by Results (national tariff)

    Based on hospital returns within specific HRGs

    Provides published unit costs for day cases, elective and emergency procedures etc.
  - Personal Social Services Research Unit (PSSRU)

    Unit costs of health and social care
  - British National Formulary (BNF)
- Direct valuation (e.g. patient expenses – travel, time, OTC)

  Questionnaires

  Diaries

Health outcomes

Identify → Measure → Value outcomes

- Disease specific outcomes - focuses on health outcomes specific to: an individual disease, an identified population

- Limitations → Not a comprehensive measure of health & QoL
  Narrow focus on disease endpoints, clinical significance unclear *(e.g. cost per toenail fungal infection averted)*

- Not possible to compare disease specific outcomes across conditions/programmes

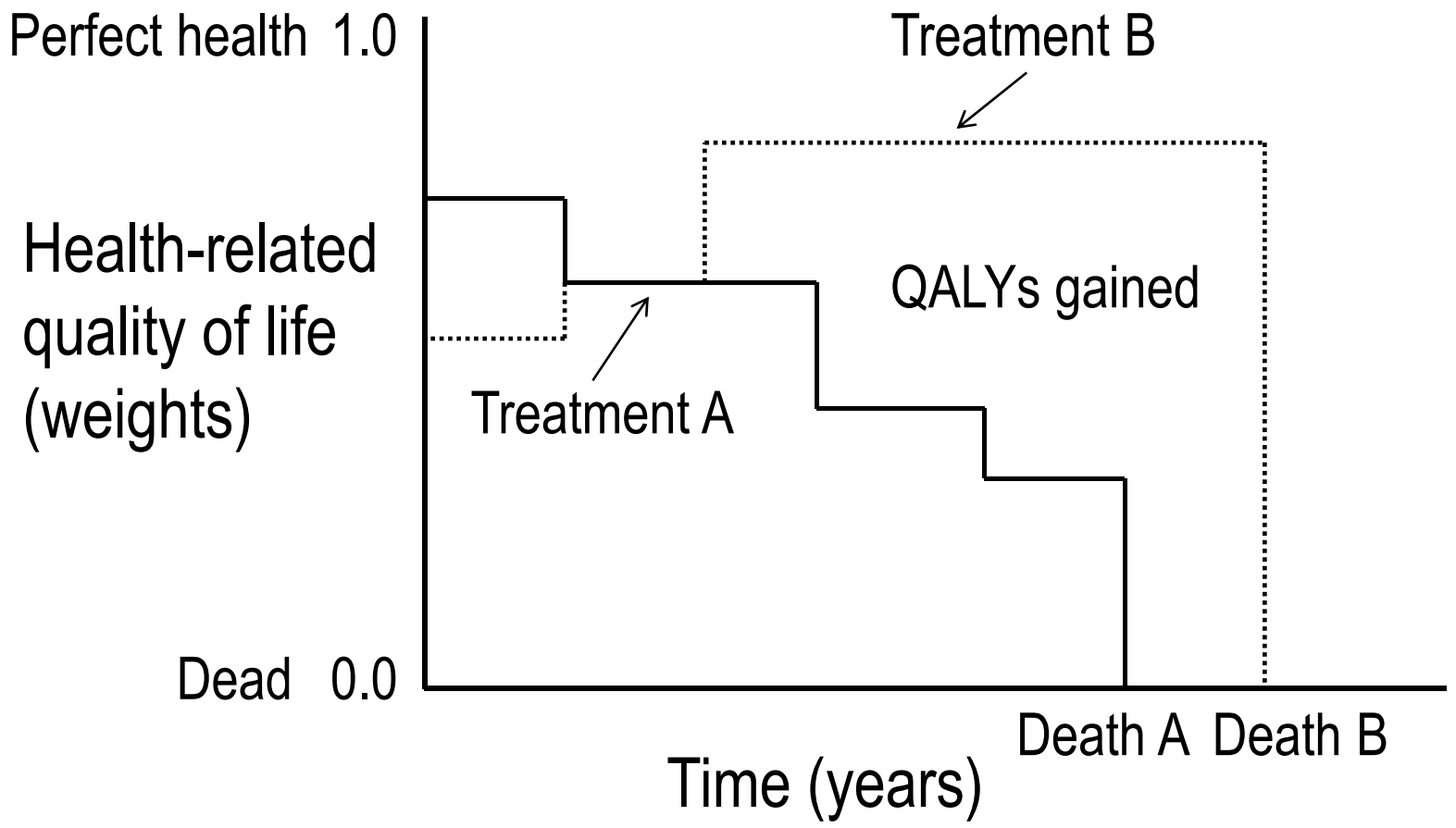
Health outcomes

- Generic measure of quality of life
  - Physical functioning,
  - Social functioning,
  - Pain
  - Psychological well-being
  - Vitality
- Intervention affects both morbidity and mortality
- Comparison across different health care programmes

Priority setting in health care (opportunity cost) → Compare added QALYs with QALYs lost from displaced programmes

Quality-adjusted life years (QALYs)

- Combines gains from reduced morbidity (quality) and mortality (quantity) into a single measure



QALY weights (utilities)

- Preference elicitation
  - Visual analogue scale
  - Time trade off
  - Standard Gamble
- Mapping onto health state measures for which preferences are known e.g. EQ-5D
  - Mobility
  - Self-care
  - Usual activity
  - Pain / discomfort
  - Anxiety / depression

Describing your own health today

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility
- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Self-Care
- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual Activities (e.g. work, study, housework, family or leisure activities)
- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/Discomfort
- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/Depression
- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

3 levels, 5 attributes =

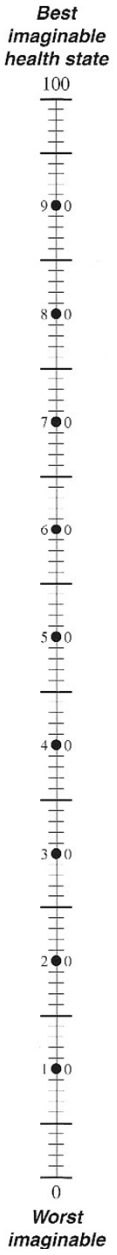
3^5 + death + unconscious = 245 health states

Valuing your own health today

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



EQ-5D scoring formula

Coefficients for TTO tariffs

Dimension	Coefficient
Constant	0.081
Mobility	
level 2	0.069
level 3	0.314
Self-care	
level 2	0.104
level 3	0.214
Usual activity	
level 2	0.036
level 3	0.094
Pain/discomfort	
level 2	0.123
level 3	0.386
Anxiety/depression	
level 2	0.071
level 3	0.236
N3	0.269

From Dolan *et al*. (1995), Table 1.

Value elicitation methods

Value sets use TTO methods and EQ-5D VAS (harmonized, European VAS value set)

Note: Algorithm for computing the tariff, subtracting the relevant coefficients from 1.000 (full health)

Key assumptions about individual preferences

1) Constant proportional trade-off

   *e.g. 10 years in a health state with a utility of 0.4 (10*0.4 = 4 QALYs) is equivalent to 5 years in a health state with a utility of 0.8 (5*0.8 = 4 QALYs)*

2) Additive independence in preferences

   e.g. 5 years in health state A followed by 8 years in health state B is equivalent to 8 years in A followed by 5 years in B

3) Equity – In aggregating, a QALY's worth of health represents the same value whoever receives it

7. WERE COSTS AND CONSEQUENCES ADJUSTED FOR DIFFERENTIAL TIMING?

- We are not indifferent to *when* costs are incurred or benefits obtained
- The procedure used in economic evaluation is *to discount* costs and benefits occurring in the future *to present values*
- Future costs and benefits given less weight than present costs and benefits
- Discount rate (usually determined by the Treasury)
- UK 3.5% per annum for both costs and benefits

8. WAS AN INCREMENTAL ANALYSIS OF COSTS AND CONSEQUENCES OF ALTERNATIVES PERFORMED?

- In comparing two options we want to assess what *extra* benefits we incur for any *extra* costs
- The traditional analytic tool of CEA is the incremental cost-effectiveness ratio (ICER)

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{\text{Cost of new treatment} - \text{cost of standard treatment}}{\text{Effect of new treatment} - \text{effect of standard treatment}}$$

Decision rules:

The league table rule: Select programmes in ascending order of the ICER until resources are exhausted

The threshold ICER rule: Select programmes with ICER $\leq \lambda$

How UK NICE says it makes decisions:

6.3.3 Above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of the technology as an effective use of NHS resources will specifically take account of the following factors:

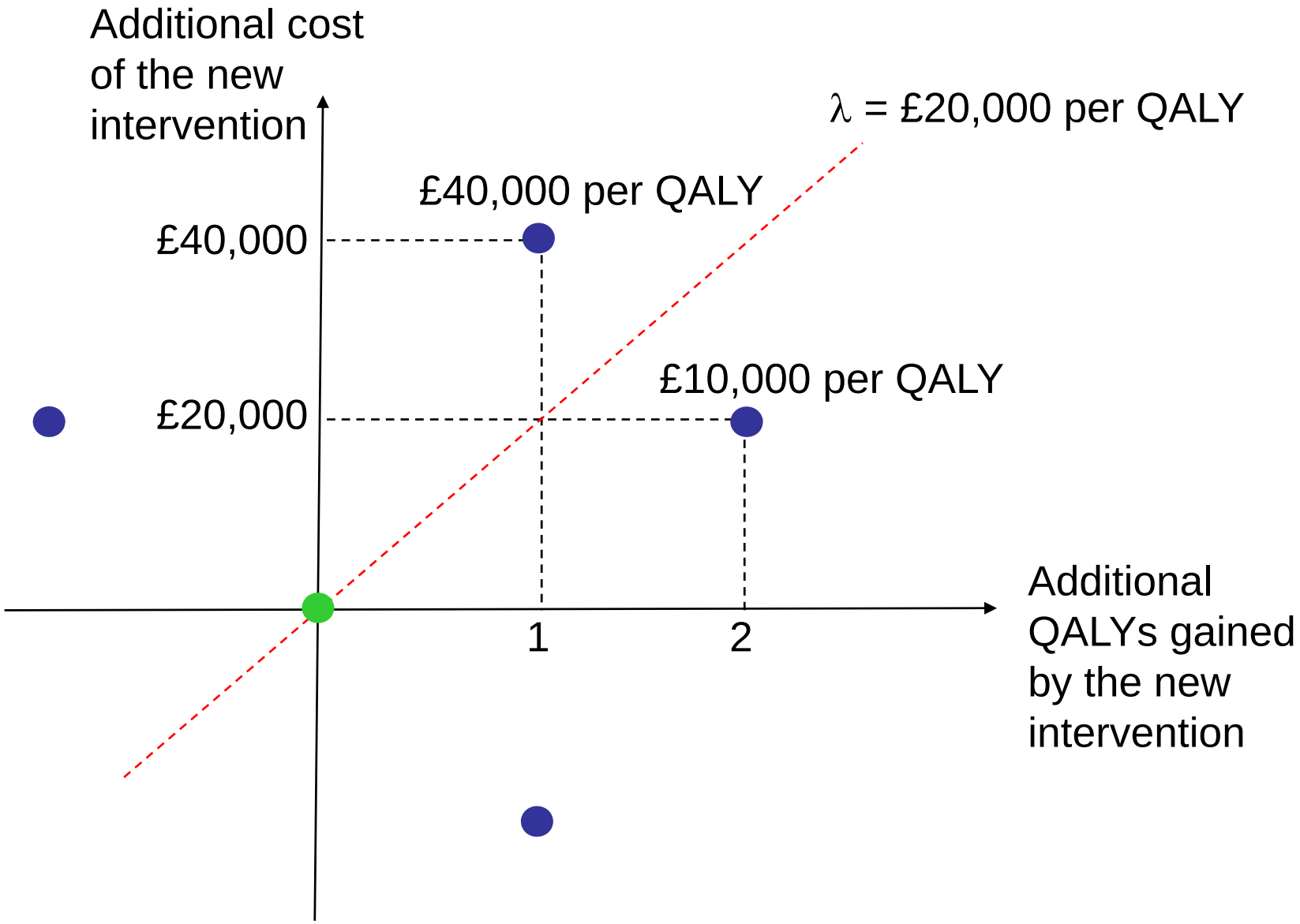
- The degree of certainty around the ICER. In particular, the Committee will be more cautious about recommending a technology when they are less certain about the ICERs presented.
- Whether there are strong reasons to indicate that the assessment of the change in health-related quality of life has been inadequately captured, and may therefore misrepresent the health utility gained.
- The innovative nature of the technology, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the reference case QALY measure.
- The technology meets the criteria for special consideration as a 'life-extending treatment at the end of life' (see section 6.2.10)
- Aspects that relate to non-health objectives of the NHS (see sections 6.2.20 and 6.2.21).

6.3.4 As the ICER of an intervention increases in the range of £20,000 to £30,000 per QALY gained, the Committee's judgement about the acceptability of the technology as an effective use of NHS resources will make explicit reference to the relevant factors listed in section 6.3.3.

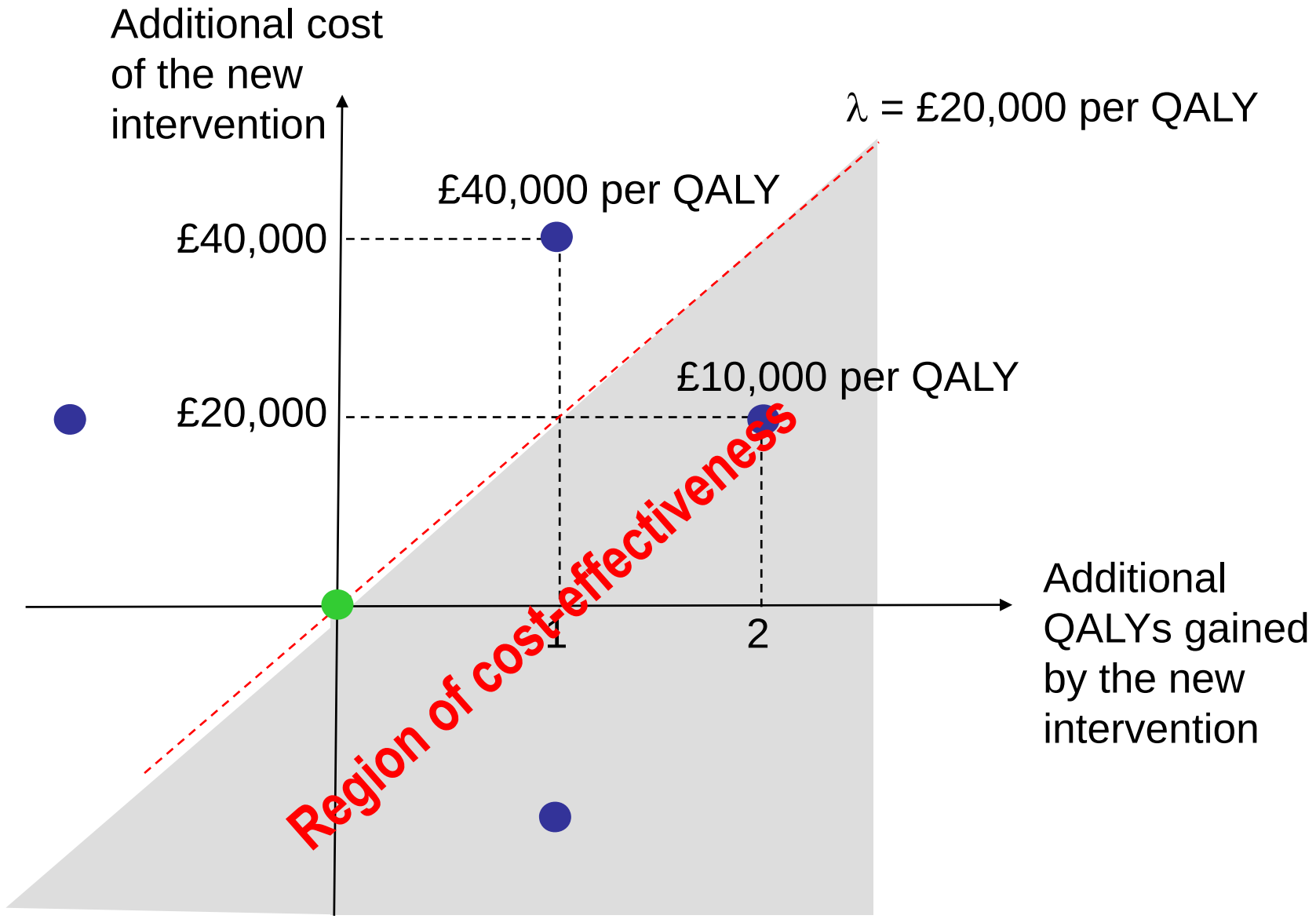
6.3.5 Above a most plausible ICER of £30,000 per QALY gained, the Committee will need to identify an increasingly stronger case for supporting the technology as an effective use of NHS resources, with regard to the factors listed in section 6.3.3.

Source: National Institute for Health and Care Excellence (NICE). *Guide to the Methods of Technology Appraisal*. London: NICE, 2013.

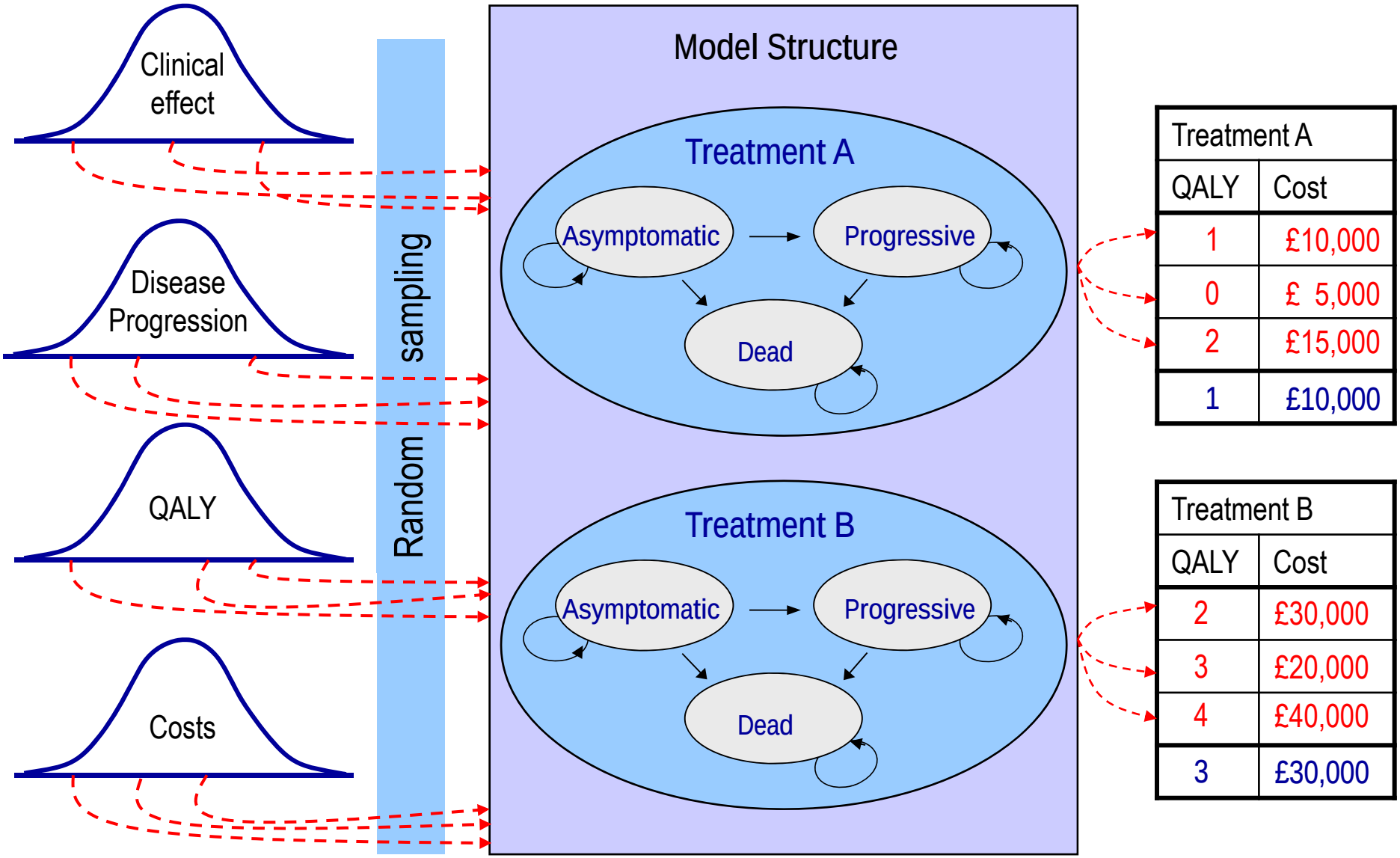
Cost-effectiveness plane



Cost-effectiveness plane



Bringing everything together



Treatment A	
QALY	Cost
1	£10,000
0	£ 5,000
2	£15,000
1	£10,000

Treatment B	
QALY	Cost
2	£30,000
3	£20,000
4	£40,000
3	£30,000

Should the intervention be adopted?

Treatment A	
QALY	Cost
1	£10,000
0	£ 5,000
2	£15,000
1	£10,000

Treatment B	
QALY	Cost
2	£30,000
3	£20,000
4	£40,000
3	£30,000

$$\text{ICER} = \frac{\text{Additional cost}}{\text{QALYs gained}} = \frac{£20{,}000}{2\ \text{QALYs}} = £10{,}000\ \text{per QALY}$$

Is the ICER less than the cost-effectiveness threshold?

£10,000 per QALY < £20,000 per QALY

→ Treatment B is cost-effective

Is net benefit positive?

Net money benefit = £ value of QALYs gained – additional costs

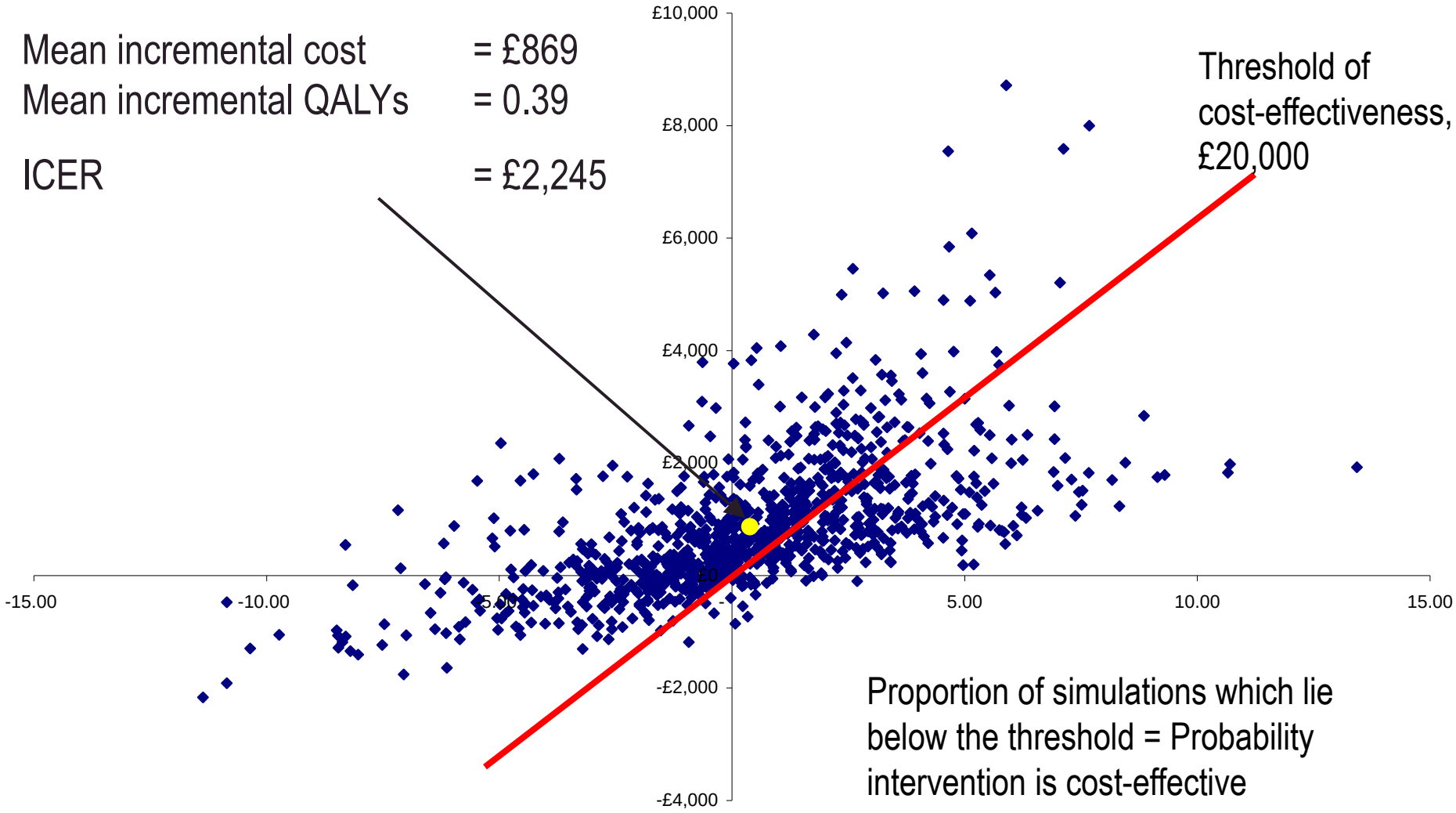
= 2 x £20,000 – £20,000

= £20,000 = 1 QALY > 0

9. WAS ALLOWANCE MADE FOR UNCERTAINTY IN THE ESTIMATES OF COSTS AND CONSEQUENCES?

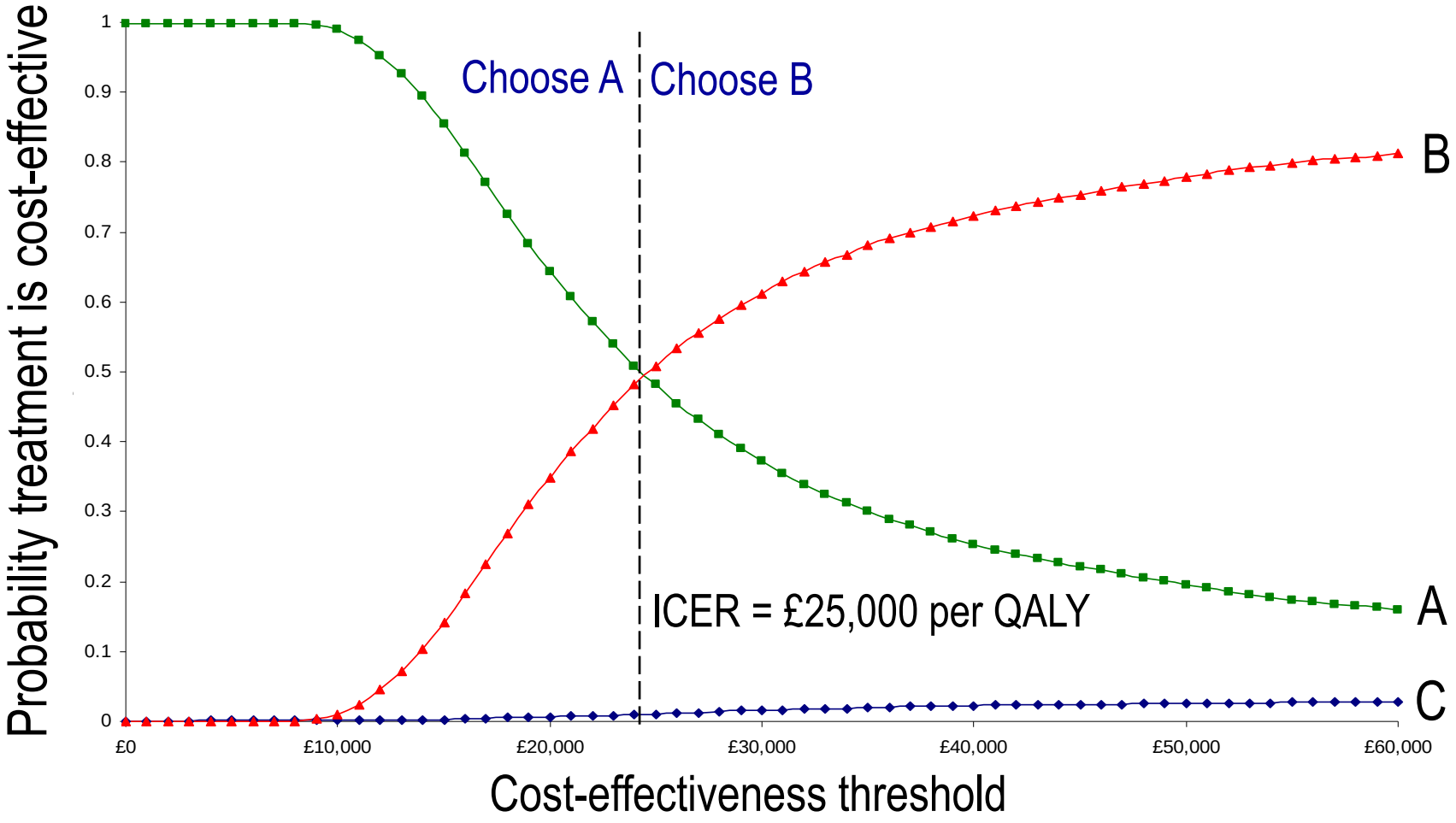
- Estimates are rarely known precisely
- Sensitivity analysis (vary parameter inputs and assumptions to see whether the results change the decision)
  - One-way sensitivity analysis
  - Multi-way sensitivity analysis
  - Probabilistic sensitivity analysis
  - Threshold analysis

Cost-effectiveness plane: Probabilistic sensitivity analysis



Cost-effectiveness acceptability curve (CEAC)

- Illustrates the uncertainty around the estimate of cost-effectiveness
- Shows the probability that one treatment is cost-effective relative to the alternative treatments for a range of threshold values



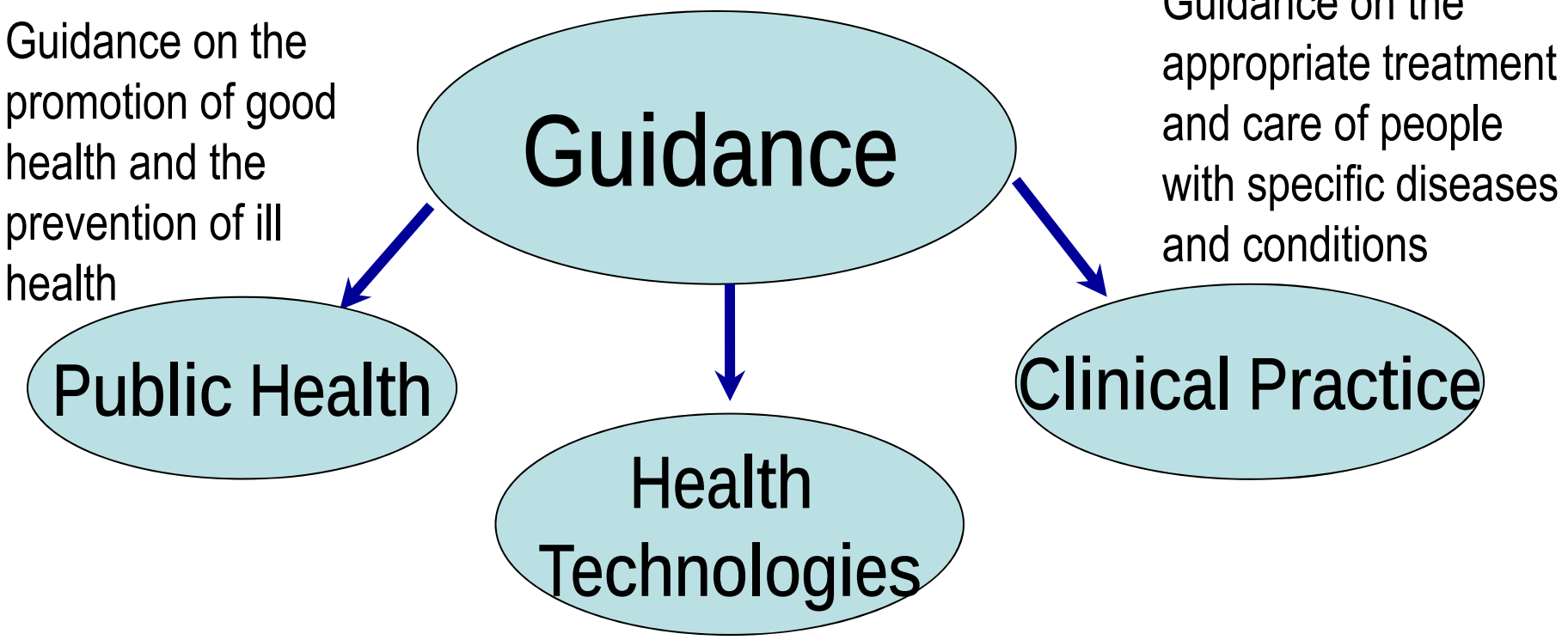
10. DID THE PRESENTATION AND DISCUSSION OF STUDY RESULTS INCLUDE ALL ISSUES OF CONCERN TO USERS?

- Was the decision problem addressed?
- Reliability, relevance and generalisability of study results
- Uncertainty – Is additional evidence required?
- Variability and heterogeneity, subgroup of patients

National Institute for Health and Care Excellence (NICE)

http://www.nice.org.uk/

NICE guidance



Guidance on the use of new and existing medicines, treatments, procedures, medical technologies and diagnostics. They consider the clinical and cost-effectiveness of the technologies

Core principles of all NICE guidance

- Based on the best evidence available
- Expert input
- Patient and carer involvement
- Independent advisory committees
- Genuine consultation
- Regular review
- Open and transparent process

Source: NICE, http://www.nice.org.uk/

Technology appraisals

- Technology appraisal recommendations are based on a review of clinical and economic evidence
- **Clinical effectiveness evidence** measures how well the medicine or treatment works in terms of clinical endpoints
- **Economic evidence** measures how well the medicine or treatment works in relation to how much it costs the NHS - does it represent value for money?
- Independent academic assessment group reviews the evidence submission presented by the manufacturer and develops their own submission for MTA appraisals
- Obligation for NHS organisations to fund and resource medicines and treatments recommended, usually within three months of NICE issuing guidance

Source: NICE, http://www.nice.org.uk/

Technology appraisal process

1. Provisional appraisal topics chosen
   -The Department of Health (DH) produces a list of provisional appraisal topics
2. Consultees and commentators identified
3. Scope prepared
   -The scope defines the disease, the patients and the technology covered by the appraisal
   -Consultees and commentators are requested to comment on the draft scope
4. Evidence submitted
   -The manufacturer or sponsor of the technology is invited to provide evidence submission
5. Evidence Review Group (ERG) report prepared (STAs)
   -NICE commissions an independent academic centre to technically review the evidence submission and prepare an ERG report

   Independent Assessment Group (AG) report prepared (MTAs)
   -NICE commissions an independent academic centre to technically review the evidence submission by the manufacturer or sponsor and prepare an independent report that reviews published evidence on clinical and cost-effectiveness of the technology

Source: NICE, http://www.nice.org.uk/

Technology appraisal process

6. Evaluation report prepared
   -This includes all of the evidence that will be looked at by the Appraisal Committee

7. Appraisal Committee
   -An independent advisory committee considers the evaluation report and hears evidence from nominated clinical experts, patients and carers.
   Committee discussions are held in public.

8. Appraisal consultation document (ACD) if produced
   -The Appraisal Committee make its provisional recommendations in the ACD. An ACD will be produced only if the recommendations from the Appraisal Committee are restrictive.
   Consultees and commentators have 4 weeks to comment on the ACD.

9. Final appraisal determination (FAD) produced
   -The Appraisal Committee considers the comments on the ACD if produced, then makes its final recommendations in the FAD on how the technology should be used in the NHS in England and Wales.

10. Guidance issued
    -If there are no appeals, or an appeal is not upheld, the final recommendations are issued as NICE guidance.

Source: NICE, http://www.nice.org.uk/

Difficult decisions…..

I won't let Daddy die

Girl of six raises £4,000 for life-saving drugs the NHS won't provide

By Lucy Laing

FACED with the prospect of losing her father to cancer, Chantelle Hill reacted a little differently to the average six-year-old.

Instead of letting the grown-ups deal with it, she decided to save him herself.

Now, she has raised more than £4,000 to buy the life-saving drugs David Hill needs after he was told they were not available to him on the Health Service.

The little girl made posters bearing the words, 'Please help me to save my daddy' and plastered them all over her home town of Darlington.

Her mother Tina, 46, said: 'We are so proud of Chantelle. She worships her dad…

Clinical Excellence found it was not 'an effective use of NHS resources'.

The £4,000 Chantelle has raised will pay for only two months of treatment, but she is determined to keep going and raise more, Mrs Hill said.

Mr Hill, 45, a builder, was diagnosed with lung cancer in December 2004.

A few months later he had an operation at the James Cook Hospital in Middlesbrough to remove the tumour from his right lung.

The father of four then had 14 weeks of chemotherapy to kill off any remaining cancer cells.

Mrs Hill said: 'Chantelle really kept him going – she's a real daddy's girl.

He absolutely dotes on her and it gave him strength to fight through with her just being there. He would still help her with her homework and…

Doctors then told the couple that Mr Hill wouldn't be able to cope with any more chemotherapy as he had lost three stone and his body was too weak. His only hope was Tarceva.

Although it is not a cure, Tarceva has been shown to extend the lives of patients with cancers such as Mr Hill's and to improve their quality of life. It has been welcomed by cancer specialists around the world and is used extensively in Europe and the US.

Mrs Hill said: 'The doctors said we would lose David if he had any more chemotherapy treatment, so we couldn't risk that.

To be told there was a drug that could keep him alive, but it wasn't funded by the NHS was just devastating.'

BBC NEWS CHANNEL

Page last updated at 14:00 GMT, Tuesday, 13 May 2008 15:00 UK

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Hero helps others fight for cancer drug

By Graham Satchell
BBC Breakfast Reporter

Kate Spall has become an unlikely hero. A 36-year old housewife from Chester, she's become a life-saver to cancer patients around the country.

Life-extending cancer drugs wait for NHS approval

Kate is not a doctor, she has no medical training at all, but she's become successful at obtaining new cancer drugs for patients that have yet to be approved for use on the NHS.

Kate's journey began when her own mother was diagnosed with kidney cancer at the age of 56. Pamela Northcott was told by her hospital that there was a drug which could extend her life, but

she couldn't have it because it hadn't been assessed by the National Institute of Clinical Excellence (Nice).

"An American asked why NICE kills people"

Source: Peter Littlejohns, The Challenge of Health Care in Europe: "value for money"

The price of life: BBC documentary

http://www.adamwishart.info/2009/06/the-price-of-life-bbc-documentary.html

Revlimid® (lenalidomide)

NICE u-turn on Celgene's cancer drug Revlimid

UK NEWS / WORLD NEWS | FEBRUARY 01, 2009 SHARE 0

SELINA MCKEE Tweet

Patients in the UK with multiple myeloma were given a new ray of hope last week, after the National Institute for Health and Clinical Excellence changed its position on the use of Celgene's Revlimid on the National Health Service.

In the autumn of last year, the Institute sparked outcry from charities and patients with its recommendation to reject the use of Revlimid (lenalidomide), in combination with dexamethasone, for patients with the blood cancer MM because it was not deemed a cost-effective use of NHS resources.

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Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy

This guidance was developed using the single technology appraisal process

Key reading references

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