University of Glasgow | Institute of Health & Wellbeing

Pharmacoeconomics: from Policy to Science

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Potential conflicts of interest – none

Pharmacoeconomics: from policy to science

-Why the need for pharmacoeconomics?

-Common approaches in pharmacoeconomic evaluations

-How pharmacoeconomic evaluations inform decision-making

Workshop 1: Designing a pharmacoeconomic evaluation

Workshop 2: Decision-making based on pharmacoeconomic evidence

Seminar II Summary

Resource Allocation in Healthcare

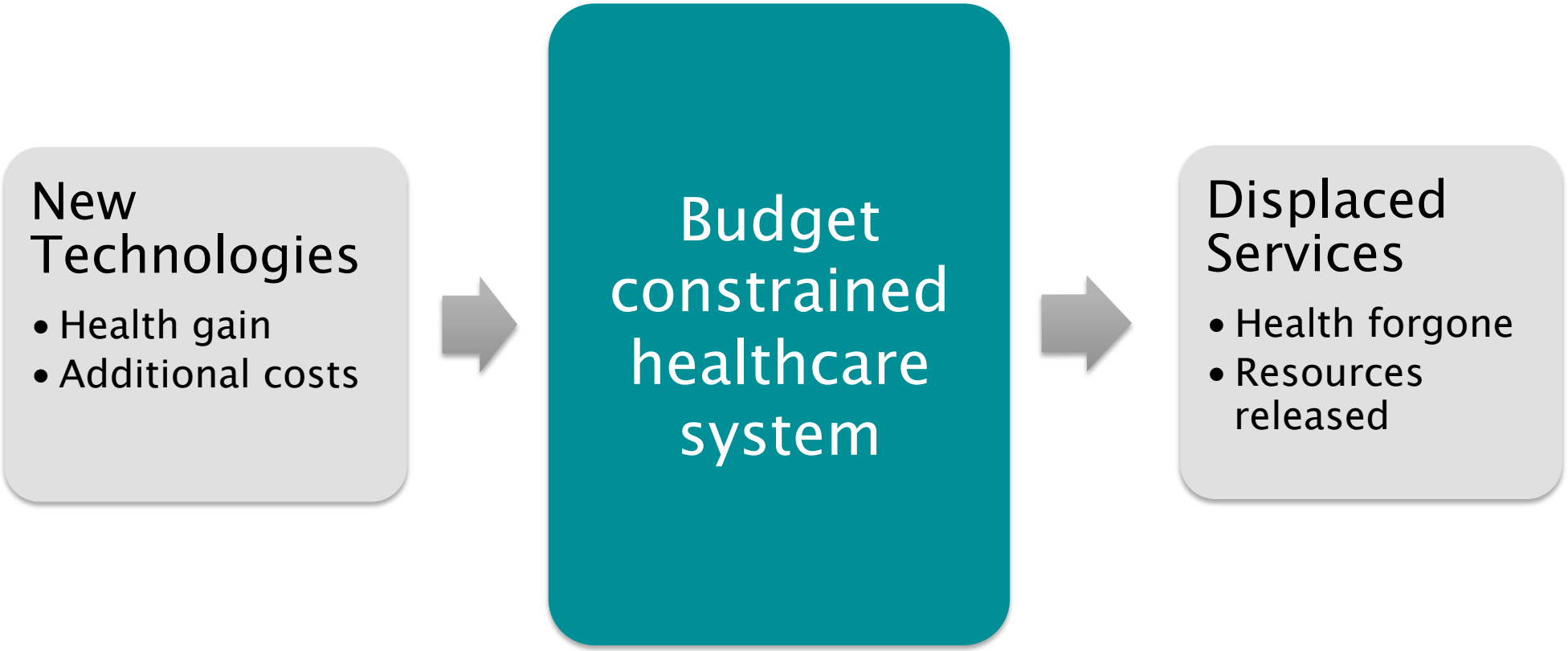
- **Budget constrained health care systems**
  - Taxation
  - Insurance
- **Systems without a budget constraint**
  - Budgets increase to accommodate new 'valuable' technologies
- **Mixed systems**
  - Budget constraints (perhaps time limited)
  - Partial increase in budget to accommodate new technologies

The 'Economic' Problem in Healthcare

- **Finite resources for health care**
- **↑ costs of health care**
  - Labour intensive
  - Expensive technologies
  - New drugs
- **↑ demand for health care**
  - Demographics
  - ↑ expectations

Priority Setting

The Concept of Opportunity Costs



Key Questions

- **Can it work?**
  - Efficacy
- **Does it work?**
  - Effectiveness
- **Should it be used, given other demands on a fixed budget?**
  - Economics

Development

EBM

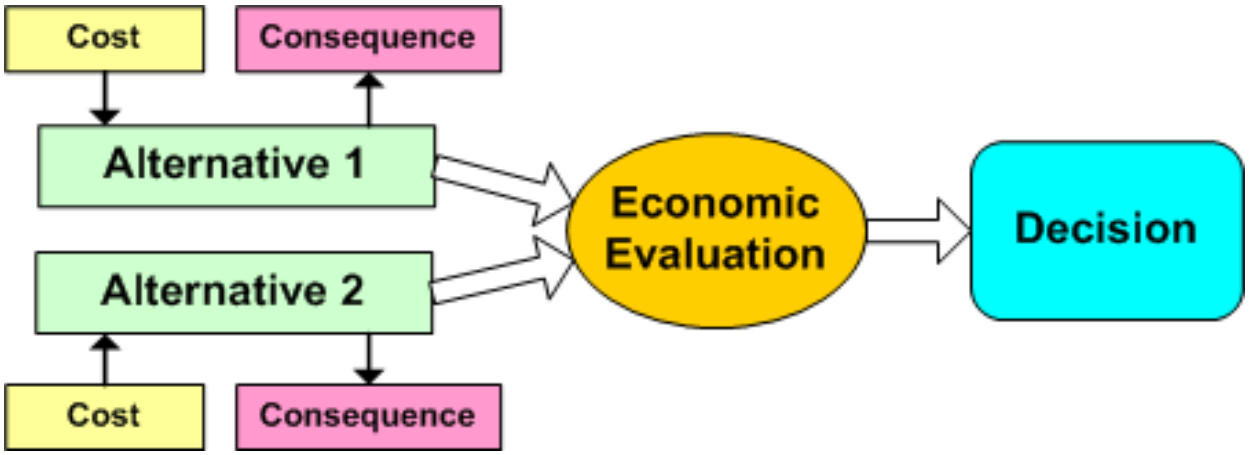
Policy

Overall Aim of Evaluation

- Help decision-makers maximise health gain (technical efficiency) given constraints
- Provide clear signals to industry regarding likely return on investment

Economic evaluation is…

" The ***comparative*** analysis of alternative courses of action in terms of both their costs ***and*** consequences in order to ***assist*** policy decisions" *(Drummond et al,1997)*



A means of comparing the virtues (benefits) and vices (costs) of different ways of doing things

Spotting Pharmaconomic Evaluations

- Is there a comparison of two or more alternatives?
- Are both costs and consequences examined?
- If not – the study is not a pharmacoeconomic evaluation but may be:
  - description of costs or outcomes
  - evaluation of efficacy or effectiveness
  - cost analysis

Stages of an Economic Evaluation

1. Define study question
   (Perspective, alternatives, form of evaluation)
2. Identify, measure and value all relevant costs and consequences
3. Adjust for differential timing
4. Apply decision rule and undertake sensitivity analyses
5. Make recommendations to decision makers

Deciding upon the study question

- Identifying the problem and aims of evaluation
  - What is the problem?
  - Why is this problem important?
  - What aspects of the problem need to be explained?
- Choosing the alternative options
  - Describing the interventions accurately
  - Defining the counterfactual intervention (comparator)
- Defining the audience
  - Defining the info needs of the audience
  - Considering how the audience will use the study results

Deciding upon the study question

- Defining the perspective of the study
  - Patient / Providers / Payers / Healthcare system / Society
  - Choosing a perspective depends on the audience
- Defining the time frame and analytic horizon
  - Analytic horizon > Time frame
- Choosing the study format
  - Prospective / Retrospective / Model
  - Depends on data, time and resources available

Types of Economic Evaluation

Cost Evaluation Types	Outcomes
Effectiveness, CEA	A common measure in natural units, different magnitudes – e.g. life years gained, mmHg change
Utility, CU	Single or multiple effects valued as "utility" – quality adjusted life years gained
Minimisation, C_{MIN}	Identical in all aspects
Benefit, CBA	Monetary
Consequence, CCA	Multiple

Cost-effectiveness Analysis (CEA)

- **If outcomes are not identical but are commensurate: $C_B/E_B > C_A/E_A$, then select A**

– lower cost per unit of output

- **E.g.**

– Smoking cessation programme (outcome – number of quitters)

– Treatments for heart conditions or cancer (outcome – years of life gained).

– Treatments to improve the quality of life (outcome – quality of life scale)

Cost Utility Analysis (CUA)

- If outcomes are multi-dimensional
  - i.e. $U_A = f(E_a, E_b, \ldots)$ and $U_B = g(E_a, E_b, \ldots)$,
  - $C_B/U_B > C_A/U_A$, then select A
  - lower cost per unit of output

- Multi-attribute quality of life (QoL) where:

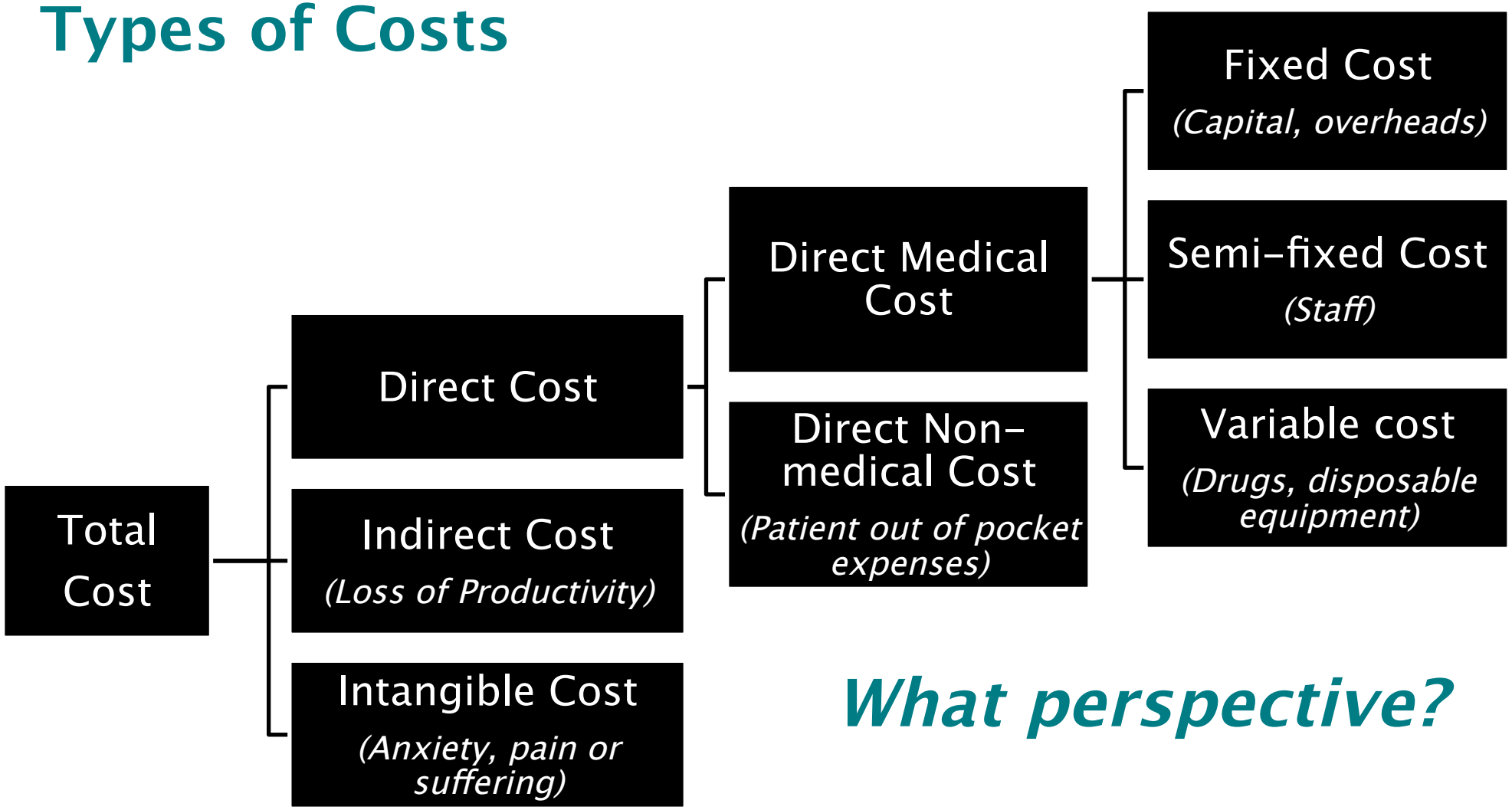
  QoL = f {physical capacities and limitations, pain, social isolation, anxiety, depression, feelings, etc.}

Cost Minimisation Analysis (CMA)

- **If outcomes are identical (i.e. non-inferior) $C_B > C_A$, then select A**
  - lower cost for given outcome

- **E.g.**
  - Post-stroke rehabilitation: home *vs.* hospital (outcome – delivery of physiotherapy)
  - Monitoring of blood pressure: self- *vs.* clinic (outcome – BP measurement)

Types of Costs



What perspective?

Measuring Costs – Precision

Most precise

Micro-costing
Each component of resource use (for example, laboratory tests, days of stay by ward, drugs) is estimated and a unit cost derived for each

Case-mix group
Gives the cost for each category of case or hospital patient. Takes account of length of stay. Precision depends on the level of detail in specifying the types of cases

Disease-specific per diem (or daily cost)
Gives the average daily cost for treatments in each disease category. These may still may be quite broad (for example, orthopaedic surgery)

Average per diem (or daily cost)
Averages the *per diem* over all categories of patient. Available in most health care systems

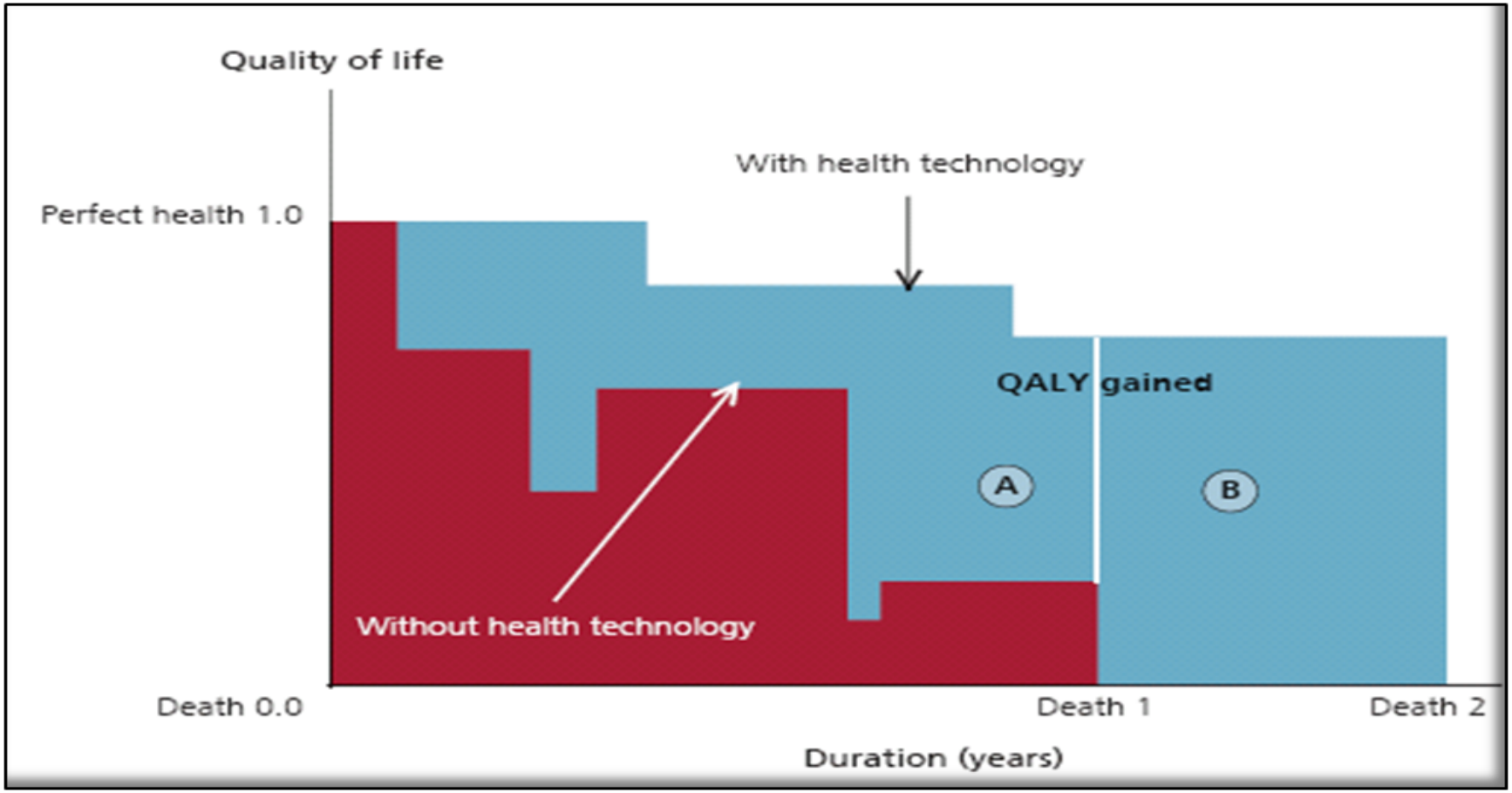
Least precise

Drummond et al, 2005

Outcomes

- **Change in health status**
  - Lives saved
  - Life-years gained
  - Measures of functioning
  - Cases avoided (preventive interventions)
- **Change in perceived health status**
  - Subjective measures of quality of life
  - Adjustment of perceived risk

Assessment of health effects



Quality Adjusted Life Years (QALYs)

- Weighting each remaining year of an individual's life by the expected quality of life
- For example:

  A 70 year old man is expected to live for another 20 years, but between the age of 80 and 90, due to a variety of illnesses, we expect his quality of life to be only half the quality of his life prior to this

(10 yrs x 1 QALY/year)

+ (10 yrs x 0.5 QALY/year) = 15 QALYs

Incremental cost-effectiveness ratio (ICER)

$$\text{ICER} = \frac{\text{Cost}_A - \text{Cost}_B}{\text{Effect}_A - \text{Effect}_B}$$

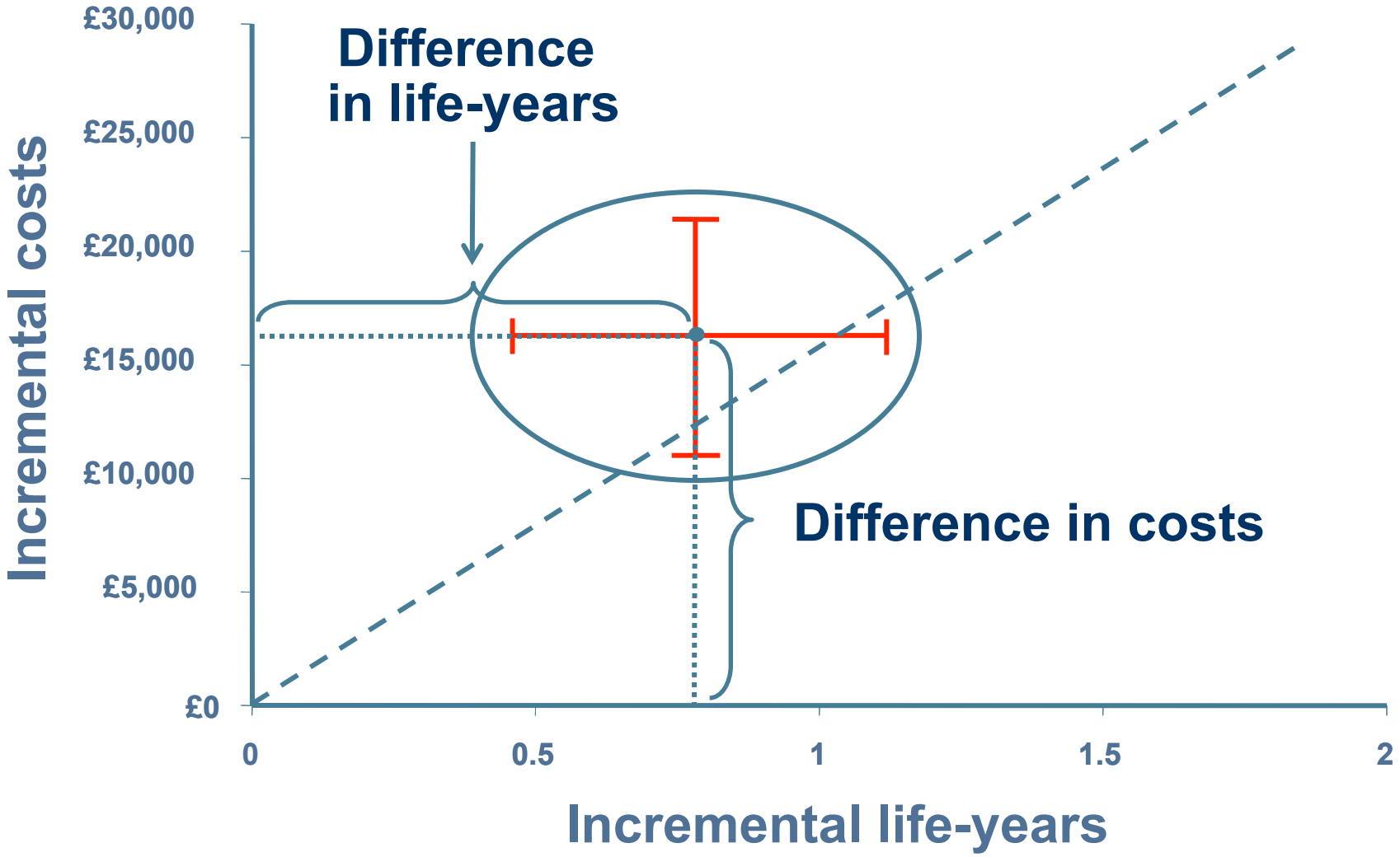
- Comparative
- Cost per unit of effectiveness (CEA)
- Cost per life-years gained (CEA)
- Cost per quality-adjusted life-years gained (CUA)

An Example

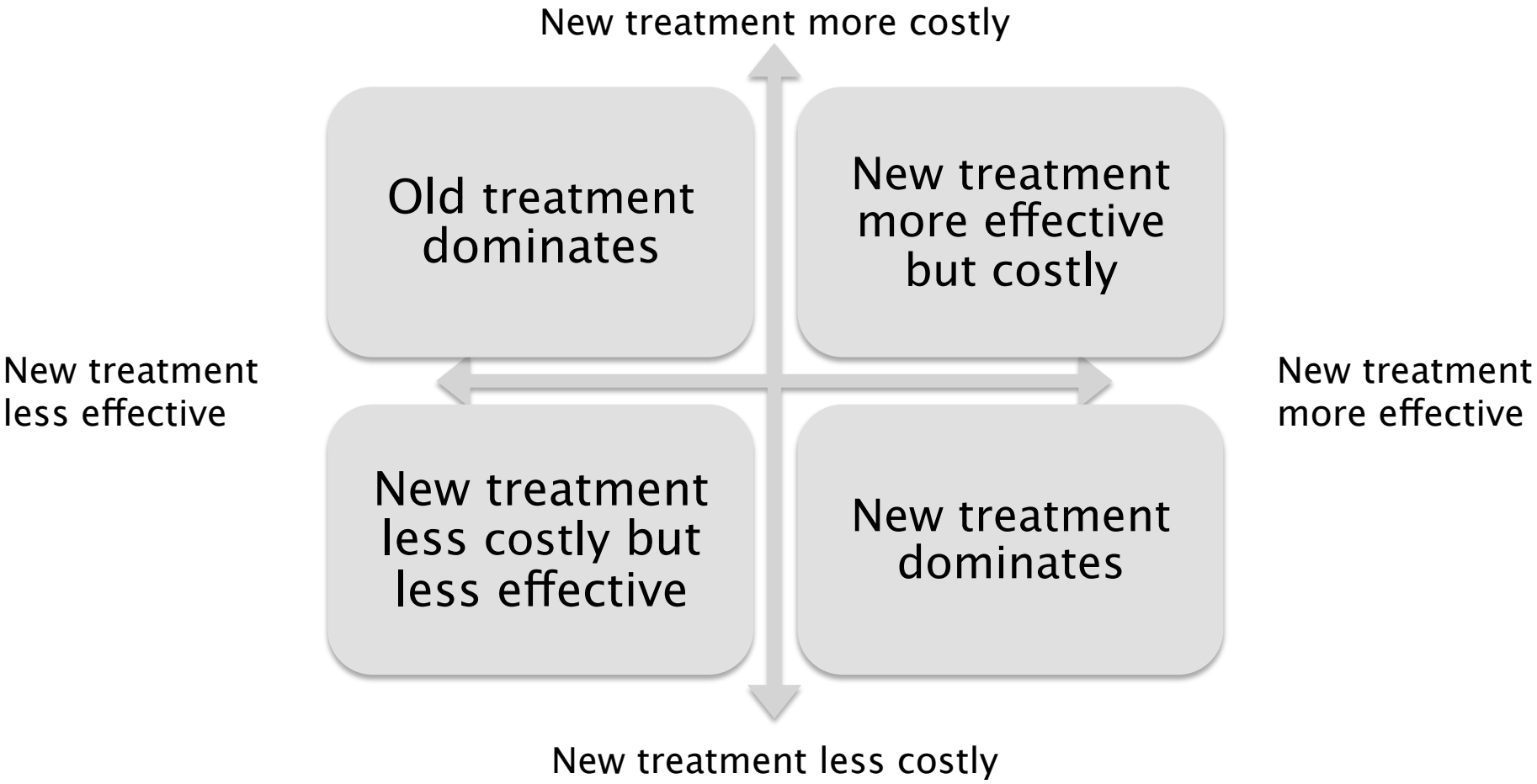
	Hip Replacement	No Hip Replacement
Quality of life (health utility)	0.7	0.5
Cost of procedure	£15,000	£0

Assumes that hip replacement patient lives for average of 15 years after intervention

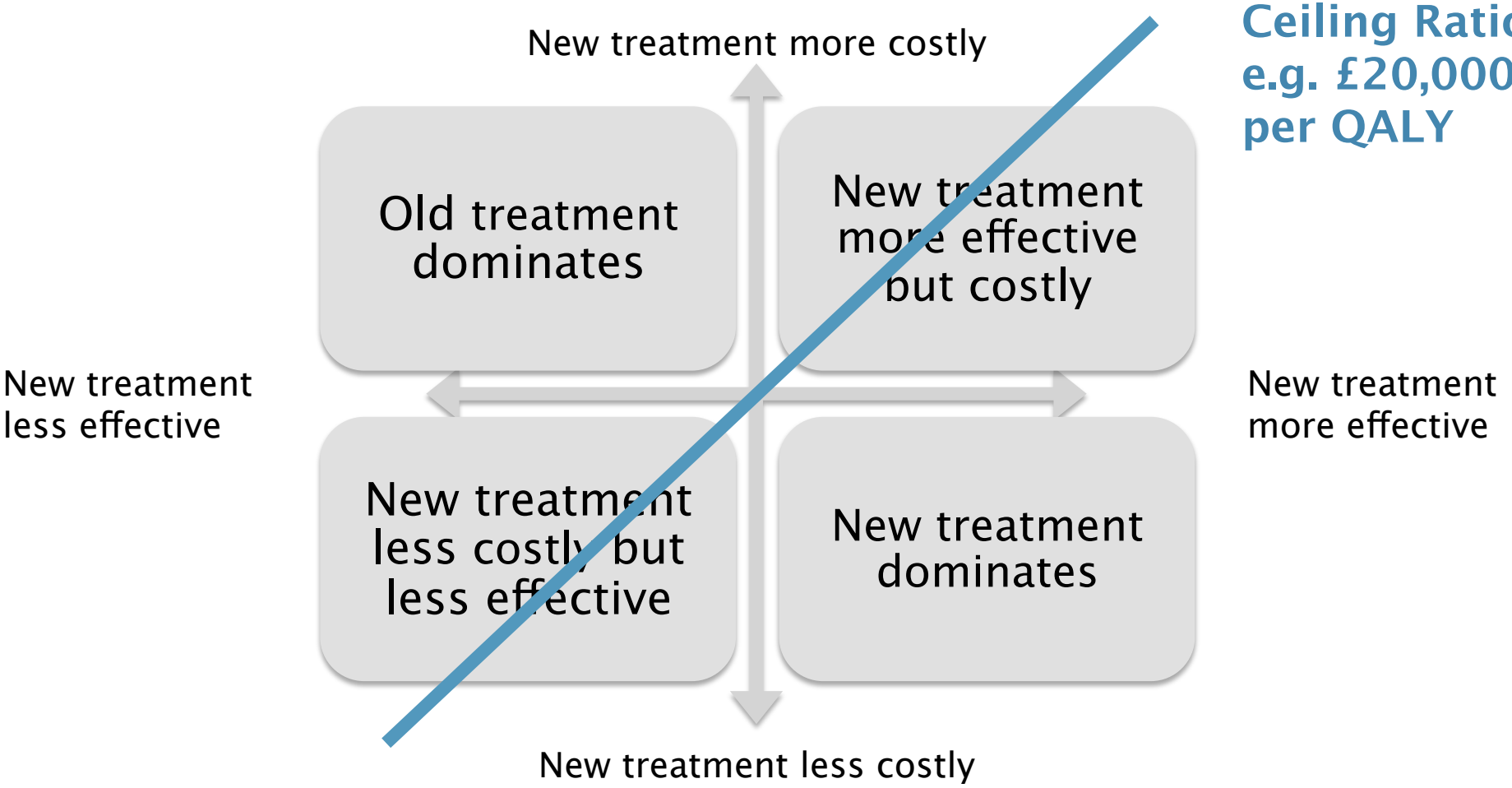
$$\text{ICER} = \frac{£15{,}000 - £0}{0.7*15 - 0.5*15} = £5000 \text{ per QALY}$$


Difference in life-years
Difference in costs
Incremental costs
£30,000
£25,000
£20,000
£15,000
£10,000
£5,000
£0
0
0.5
1
1.5
2
Incremental life-years

Incremental Cost-effectiveness Plane

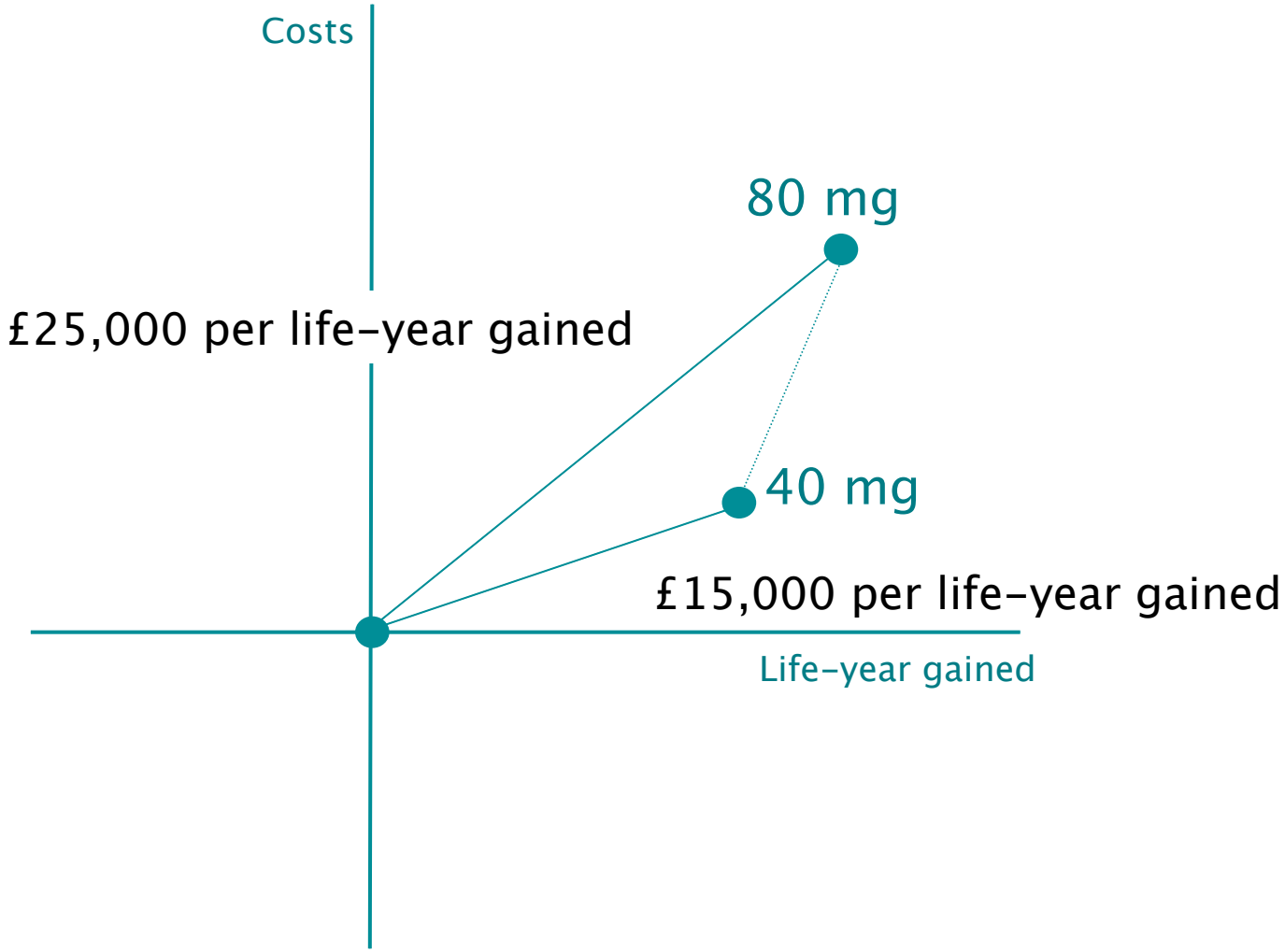


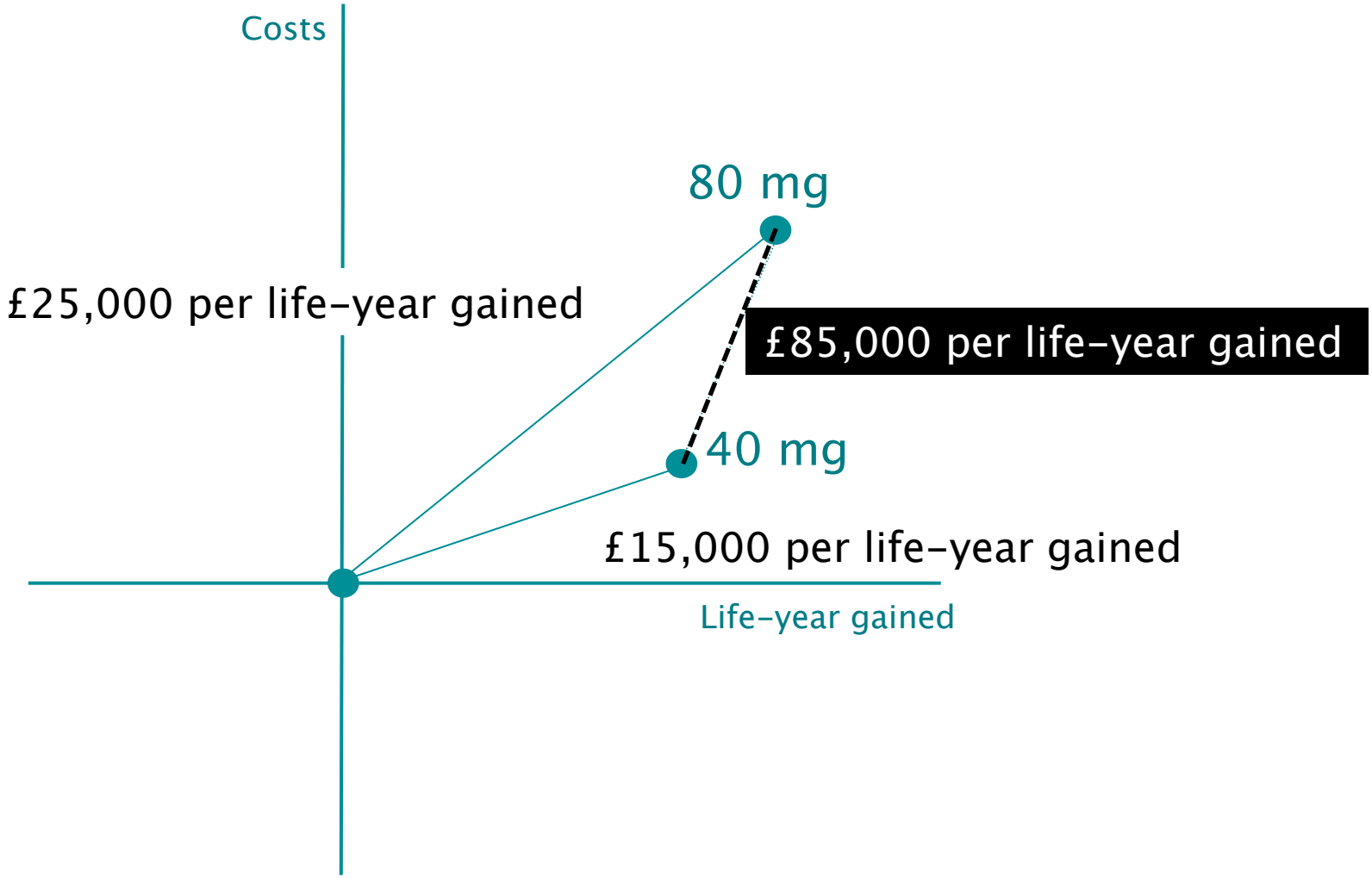
Incremental Cost-effectiveness Plane

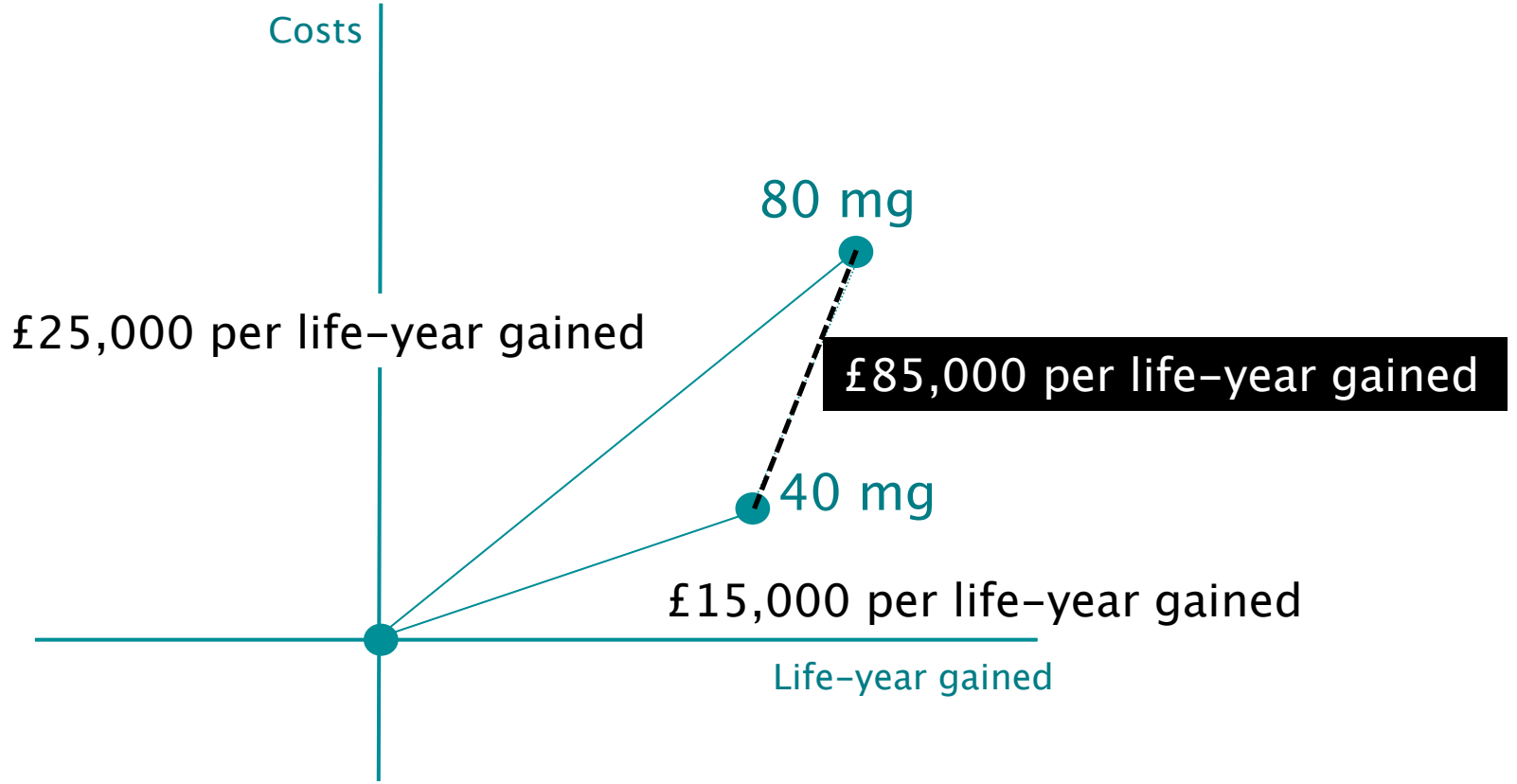


Incremental (marginal) *vs* Average Analysis?

- An analysis of different doses of a cholesterol lowering drug shows that 80mg per day gives a cost effectiveness of £25,000 per life-year gained (LYG)
- 40mg per day gives £15,000 per LYG
- So it's probably worth giving 80mg where possible as the extra LYG costs only £10,000?
- Well...


Costs
80 mg
£25,000 per life-year gained
40 mg
£15,000 per life-year gained
Life-year gained


Costs
80 mg
£25,000 per life-year gained
£85,000 per life-year gained
40 mg
£15,000 per life-year gained
Life-year gained



Incremental cost-effectiveness = what is the **additional** cost to achieve the **additional** effectiveness

Adjust for Timing – Discounting

- Prefer to have benefits now and bear costs in the future – 'time preference'
- Rate of time preference is termed 'discount rate'
- To allow for differential timing of costs (and benefits) between programmes all future costs (and benefits) should be stated in terms of **their present value** using discount rate.
- Thus, future costs given less weight than present costs.

Uncertainty and Variability

- **Overall variability between patients**
  - Observed variability within a sample of patients in, e.g. costs and outcomes
  - Reflected in standard deviations associated with a mean value
- **Parameter uncertainty**
  - Imprecision in our estimates of, e.g. mean costs or outcomes
  - Reflected in standard error of the mean
- **Sub-group heterogeneity**
  - 'Base-line' characteristics 'explain' a proportion of overall variability between patients (e.g. age, sex)
  - E.g. mean cost of an MI may differ between young and old
- **Structural (model) uncertainty**
  - Uncertainty regarding modelling assumptions

Pharmacoeconomic Evaluation

- Synthesis of available evidence: RCT, observational studies, opinion
- Extrapolation from surrogate to final endpoints
- Extrapolation over time
- Indirect comparisons
- Correction of suspected biases
- Requires assumptions and judgement
- Extrapolation = uncertainty

Iterative Approach to Economic Evaluation

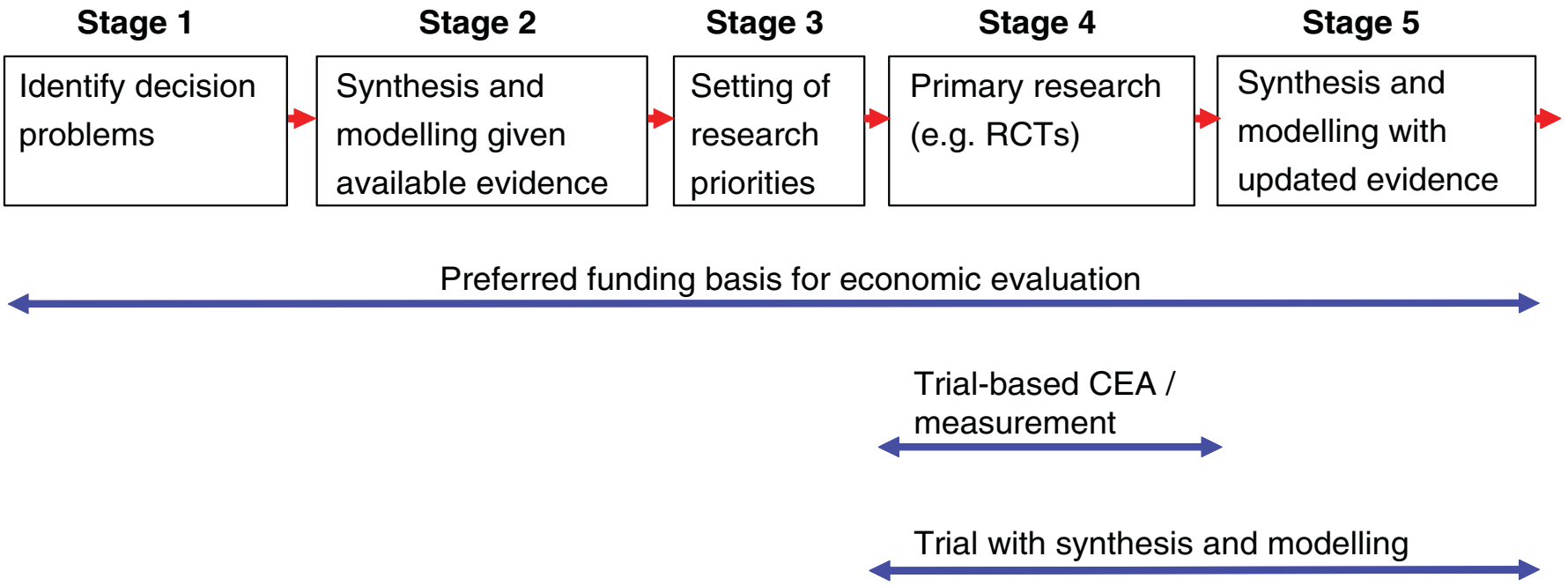


Figure 1. Five stages in an iterative approach to the economic evaluation of health technologies

Sculpher et al; Health Economics 2006
Boyd et al; Drug Dev Res 2010

Policy Decision – questions for a new technology

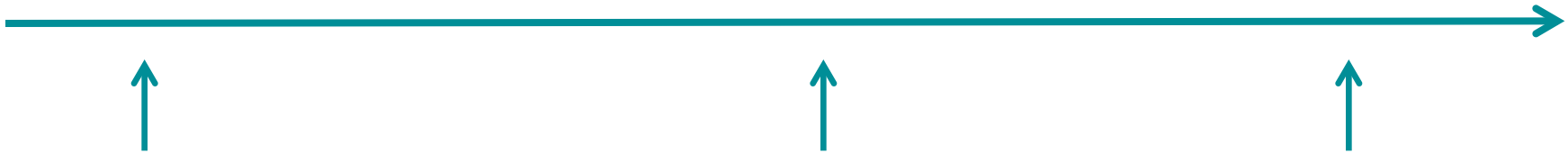
- **Does it actually work ?**
  - Is it better than the existing technology ?
  - "better" means more output, but how is output to be measured ?
- **Can we afford to pay for it ?**
  - How much will it cost ?
  - Is it worth spending more on this technology?
  - Is it worth transferring resources from another health care area to pay for this new technology?

International Guidelines on Health Technology Assessment

	Published PE Recommendations	PE Guidelines	Submission Guidelines
Africa	South Africa		
America- Centre and South		Brazil Cuba México	
America-North	United States	Canada	
Asia	China Mainland	Taiwan South Korea	Israel Thailand
Europe	Austria Denmark Hungary Italy Russian Federation Spain	Baltic (Latvia, Lithuania, Estonia) Belgium France Germany Ireland The Netherlands Norway Portugal Slovak Republic Sweden	England & Wales Finland Poland Scotland
Oceania		New Zealand	Australia

Variation in how HTA is used in decision making

Increasing use of formal quantifications of trade-offs



<u>Limited quantification</u>

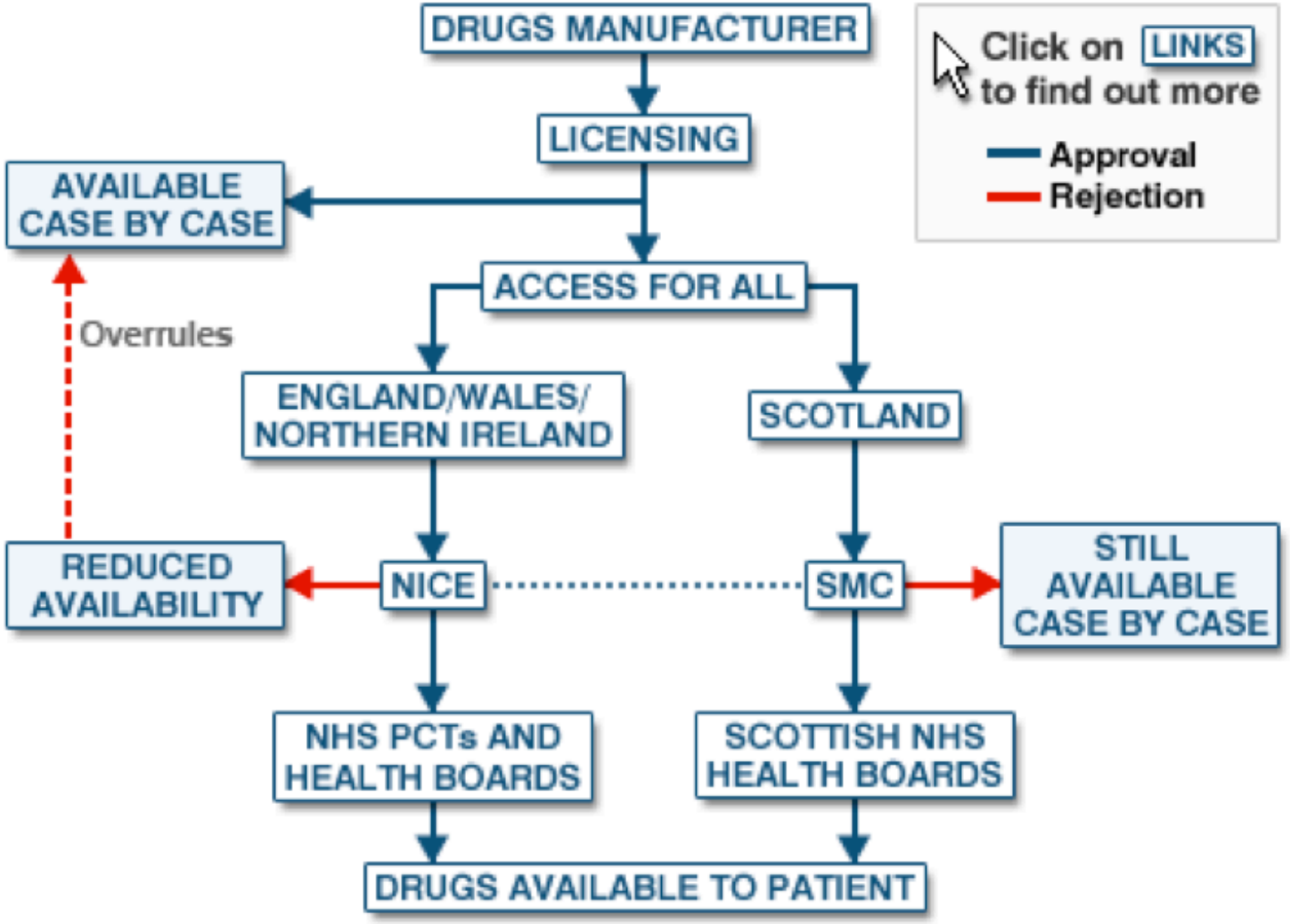
- Examples: Germany, France, US
- Focus on individual effects
- Possible interest in costs, not pharmacoeconomics

<u>Greater use of quantification</u>

- Examples: the UK, Sweden
- Interested in pharmacoeconomics
- Use of QALYs

<u>The future?</u>

- UK value-based pricing
- Weights to QALYs: severity, unmet needs, end of life



Source: http://news.bbc.co.uk/1/hi/programmes/panorama/7567998.stm

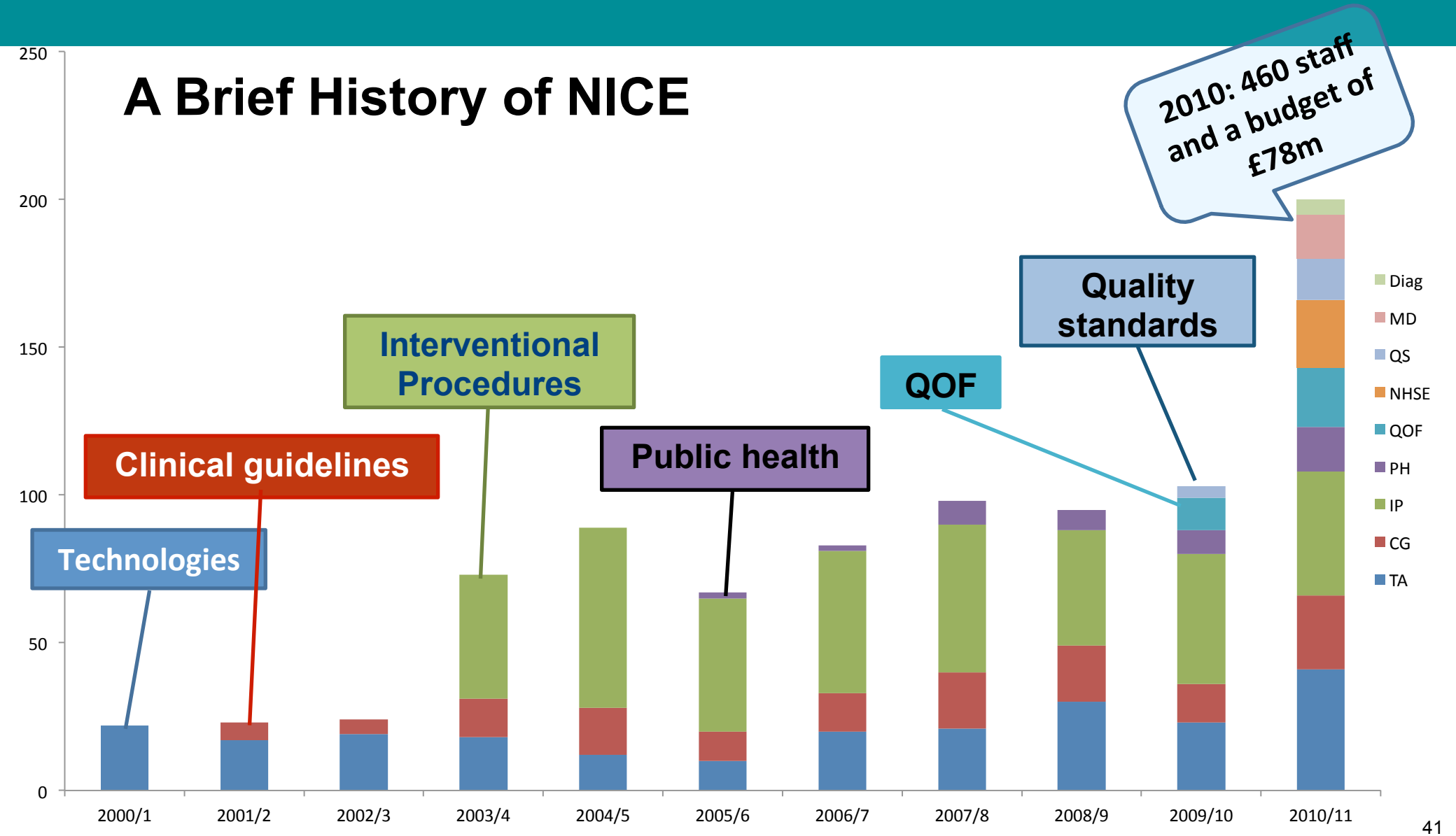
The National Institute for Health and Care Excellence

"NICE is the independent organisation in the UK responsible for providing national guidance to the NHS and the wider public health community

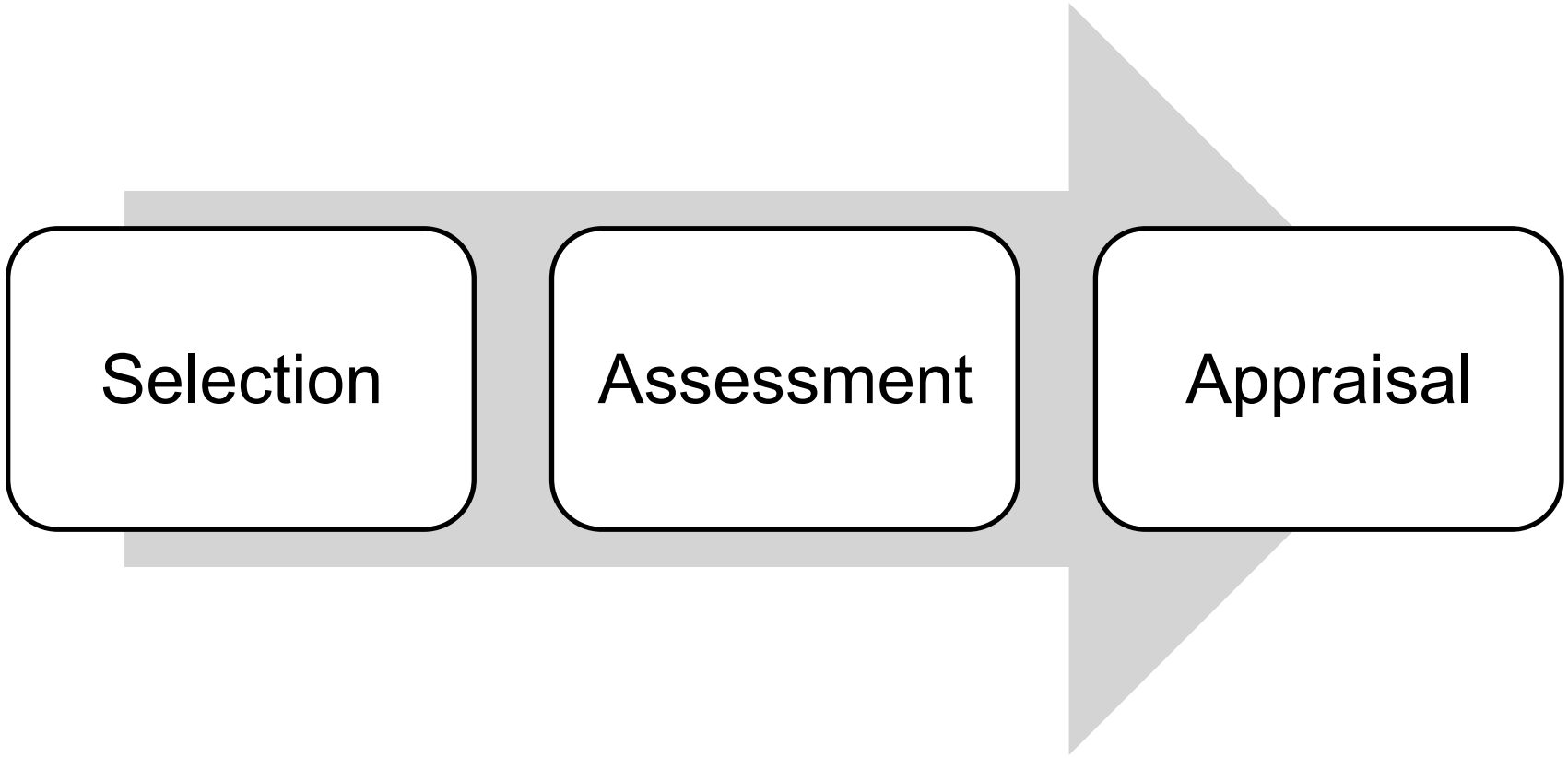
on the promotion of good health and the prevention and treatment of ill health"

- England and Wales, April 1999
- Northern Ireland, July 2006

A Brief History of NICE



The NICE Technology Appraisal Process



The NICE Process – Selection

- Not all licensed drugs selected
- NICE has key role in topic selection
- Criteria:
  - Impact on health
  - Impact on costs
  - Urgency
  - National priorities (recent predominance of cancer therapies)

The NICE Process – Assessment

- Scope sets up questions to be addressed
- Key elements of the assessment:
  - Systematic review of clinical and economic evidence
  - Cost-effectiveness analysis
  - Critical review of manufacturer submissions

The NICE Process – Assessment

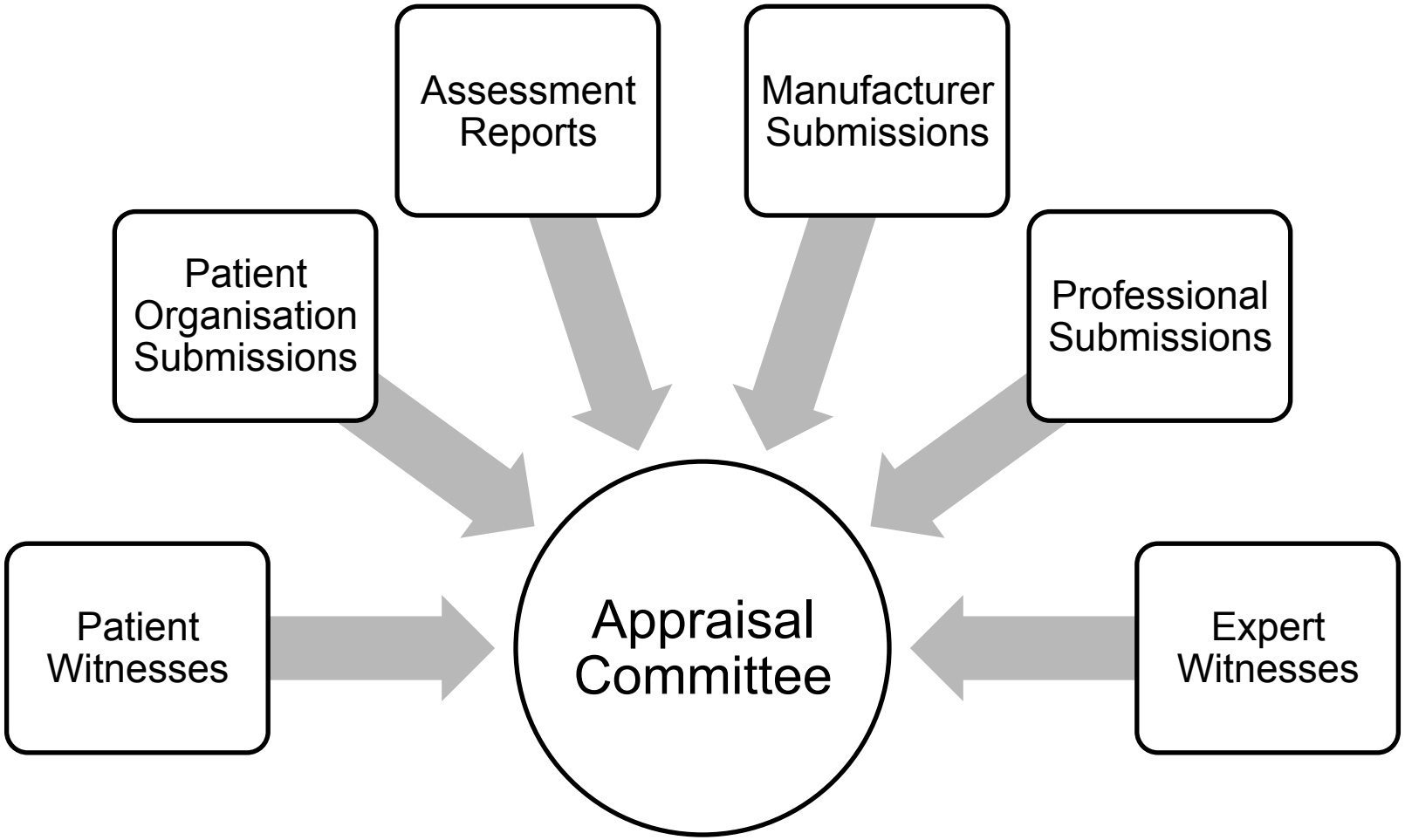
Multiple Technology Appraisals

- Several related technologies (longer review)
- Initiation to guidance about 52 weeks
- Undertaken by academic groups
- Company submissions typically include systematic review and model

Single Technology Appraisals

- Change in 2006 in face of criticism about slowness
- Relates mainly to new pharmaceuticals
- Manufacturers provide all assessment (clinical review and cost-effectiveness model)
- Academic evidence review group critically reviews submission

The NICE Process – Appraisal



The NICE Appraisal Committee Members

- Public Health Experts (x 2)
- Clinical Nurse Specialist
- Commissioning Executives (x 4)
- General Practitioner
- Health Economists (x 3)
- Statisticians (x 2)
- Clinical Pharmacologist (x 2)
- Pharmaceutical Industry (x 2)
- Lay Representative (x 2)
- CHAIR (Radiologist)
- Clinical Experts

Committee A – 28 members

The NICE Process – Decisions

- Unconditional positive guidance
- Conditional positive guidance (on particular patient characteristics)
- Negative guidance
- Recommended only in research
- Opportunity for appeal
- Decisions reviewed in the future

NICE Decision Considerations

- Weighs up benefits of technology under assessment against what's currently available
- Takes into account:
  - any undesirable side effects
  - the effects of refusing NHS availability
  - impact of treatment on length and quality of life
  - net cost to the NHS
  - the impact of treatment on NHS resources

The NICE Methods

Table 5.1 Summary of the reference case

Element of health technology assessment	Reference case	Section providing details
Defining the decision problem	The scope developed by the Institute	5.2.5 & 5.2.6
Comparator	Therapies routinely used in the NHS, including technologies regarded as current best practice	5.2.5 & 5.2.6
Perspective on costs	NHS and PSS	5.2.7 to 5.2.10
Perspective on outcomes	All health effects on individuals	5.2.7 to 5.2.10
Type of economic evaluation	Cost-effectiveness analysis	5.2.11 & 5.2.12
Synthesis of evidence on outcomes	Based on a systematic review	5.3
Measure of health effects	QALYs	5.4
Source of data for measurement of HRQL	Reported directly by patients and/or carers	5.4
Source of preference data for valuation of changes in HRQL	Representative sample of the public	5.4
Discount rate	An annual rate of 3.5% on both costs and health effects	5.6
Equity weighting	An additional QALY has the same weight regardless of the other characteristics of the individuals receiving the health benefit	5.12

HRQL, health-related quality of life; NHS, National Health Service; PSS, personal social services; QALYs, quality-adjusted life years.

NICE 2008. Guide to the Methods of Technology Appraisal

The cost-effectiveness threshold

- "The appropriate threshold to be used is that of the opportunity cost of programmes displaced by new, more costly technologies"
- If most plausible estimate is below £20,000 per QALY gained: cost-effective use of NHS resources
- Above £20,000: are there benefits not captured by the QALY? Has quality of life aspect been adequately measured?
- Above £30,000: "... need to identify an increasingly stronger case for supporting the technology as an effective use of NHS resources"

NICE. Guide to the Methods of Technology Appraisal. London: NICE, 2008

Appraising life-extending, end of life treatments

"the impact of giving greater weight to QALYs achieved in the later stages of terminal diseases, using the assumption that the extended survival period is experienced at the full quality of life anticipated for a healthy individual of the same age"

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Page last updated at 21:02 GMT, Friday, 2 January 2009

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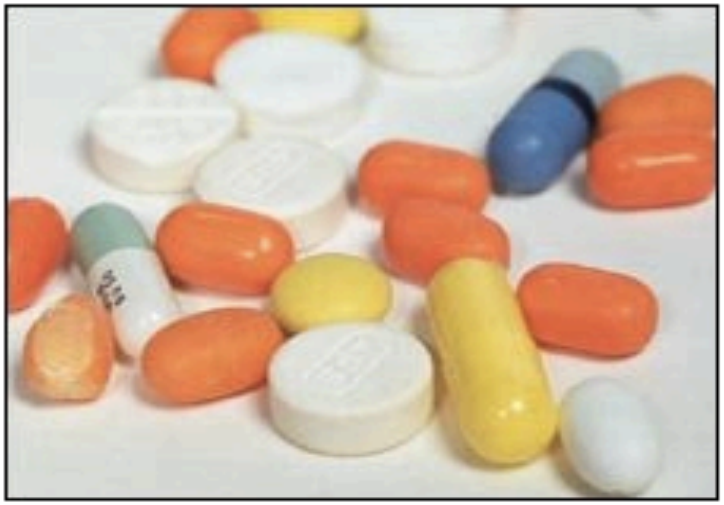
NHS end-of-life drugs rule change

Drugs which give terminally ill patients a few extra months to live have a better chance of being approved on the NHS under new rules.

The National Institute for Health and Clinical Excellence (NICE) is to extend the threshold at which the drugs are deemed cost-effective.

But this will only be in certain



The NHS has a finite pot of money for treatments

End of life criteria

- The treatment is indicated for patients with a short life expectancy, normally <24 months
- There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared to current NHS treatment
- The treatment is licensed or otherwise indicated for small patient populations

Other Threshold Exceptions

- **Severity of the underlying illness**

  When ICERs are equivalent, society would give priority to the expensive relief of a serious condition compared with relatively inexpensive relief of a mild discomfort

- **Stakeholder persuasion**

  When symptoms are poorly reflected in clinical trials or inadequately reflected in the measure of health-related quality of life used

- **Significant innovation**

  When the technology produces a substantial, demonstrable and distinct benefit, that may not have been adequately captured in the measure of health-related quality of life used

- **Disadvantaged populations**

  E.g. poorer people and ethnic minorities

- **Children**

  Society would generally favour ‘the benefit of the doubt’ being afforded to sick children

Implications of NICE Decision

- PCTs are legally bound to fund within 3 months of a positive decision
- NICE is often criticised as a “penny pinching” body to guard NHS budgets
- King’s Fund estimated NICE decisions added a net cost of £1022m to NHS budget between 2003/4 and 2006/7
- Meeting the cost of these decisions is one of the reasons PCTs often use to justify over spending

What NICE does well:

- Goes beyond HTA, provides a "front end" for the evidence produced by HTA and to integrate it with policy
- In the UK are they integrated with decision making, legally binding, national in scale and put into practice in a system with a single payment
- "*NICE's success may owe more to its setting within a single payer health system with a constrained budget than it does to anything unique about its methods*"

Criticisms of NICE

- Threshold
  - Too high
  - Too low
- Disinvestment
- Patient Perspective
- Non submission

Threshold

- Claxton K, et al. Methods for the estimation of the NICE cost effectiveness threshold (2013). University of York, Centre for Health Economics, CHE Research Paper 81.
  - A 2-year project, funded by the NIHR and MRC Methodology Research Programme
  - Aimed to develop methods to estimate the NICE cost-effectiveness threshold using routinely available data
  - "*The central or 'best' threshold is estimated to be £18,317 per QALY*"
  - Recommended additional weight for health benefits in diseases which impose a large health burden and/pr where there are wider social benefits for patients and/or carers

24 January 2013 Last updated at 23:59

Researchers claim NHS drug decisions 'are flawed'

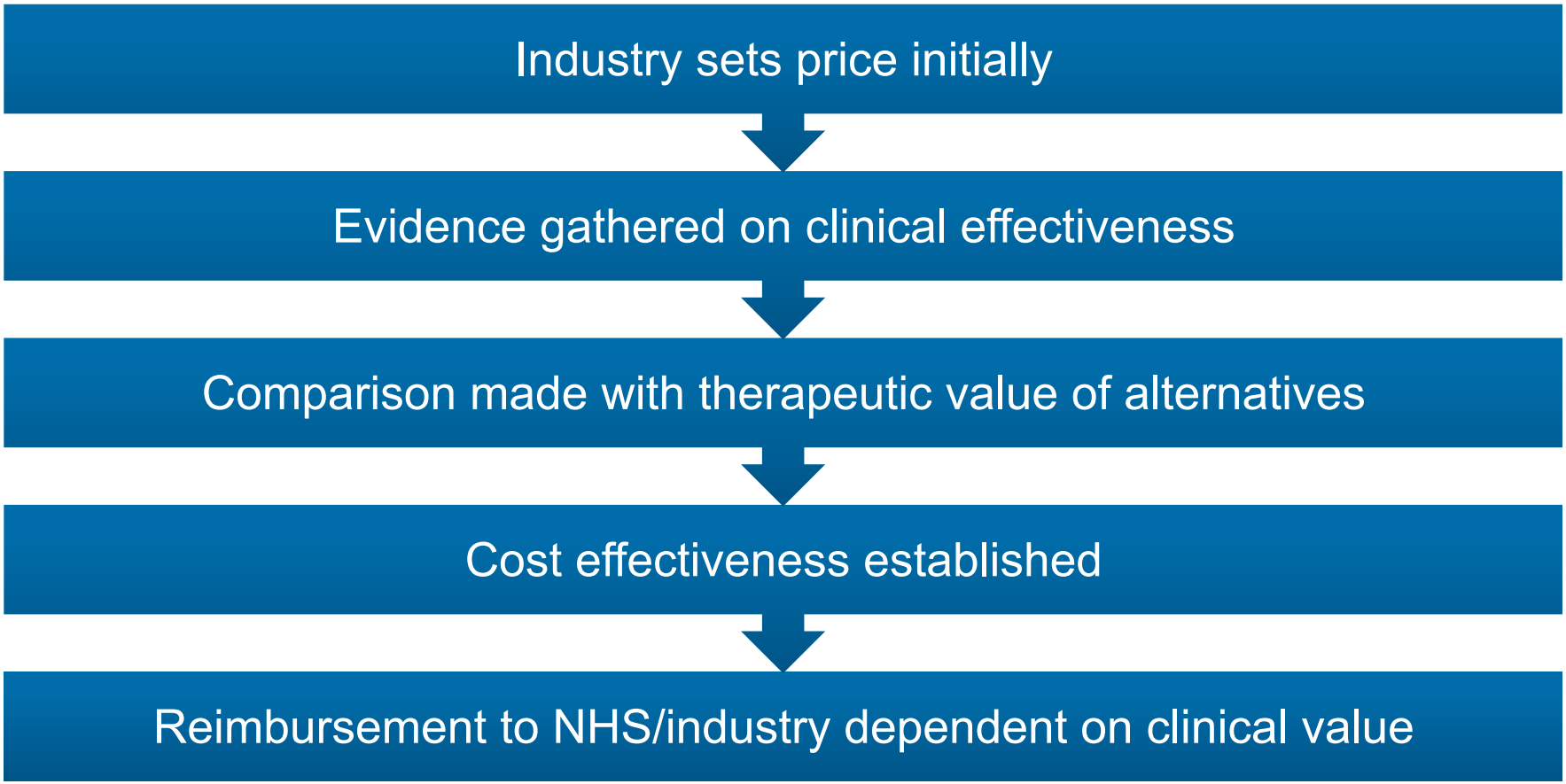
By Jane Dreaper
Health correspondent, BBC News

The formula used by the NHS to recommend which drugs should be funded is "flawed" and should be scrapped, researchers say.

The European Commission-funded study tested the assumptions of the system used by NICE (the National Institute for Health and Clinical Excellence).

Value based pricing:

- There is currently no link between clinical guidelines, HTA and medicines pricing
- UK Government committed to changing Pharmaceutical Price Regulation Scheme (PPRS) to ensure better use of NHS resources
- Basic idea is that the price of a medicine should be related to cost effectiveness based on clinical evidence
- All branded medicines would be evaluated against alternatives including generics


Industry sets price initially
Evidence gathered on clinical effectiveness
Comparison made with therapeutic value of alternatives
Cost effectiveness established
Reimbursement to NHS/industry dependent on clinical value