HTA tools for assessing benefits and costs

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What I hope to cover…

- Some basic principles
- Types of economic evaluation
- Measuring benefits and costs
- Use of modelling in HTA
- Handling uncertainty in economic evaluation
- Adoption decisions
- Patient Access Schemes
- Practical – getting utililities

Basic principles

- Opportunity cost
- Perspective
- Incremental analysis
- Uncertainty

- Opportunity cost
  - You can only spend it once
  - What is the value of a new technology under budget restraint?
- Perspective
  - Personal
  - Societal
  - Health (and social care) system

Incremental analysis

ECONOMIC EVALUATION GIVES US:

Incremental cost effectiveness ratio (ICER)

=

$$\frac{\textbf{\textit{ADDITIONAL} COST}}{\textbf{\textit{ADDITIONAL} BENEFIT}}$$

Types of economic evaluation

- Cost consequence
- Cost minimisation
- Cost effectiveness
- Cost utility (Cost per QALY)
- Cost benefit

Costs

- PRICE is not the same as COST
- Direct costs
  - Cost of the technology
  - Time used to deliver
  - Associated testing etc.
- Indirect costs
  - Shared with other programmes (e.g. management)
- Perspective, duration and time preference are important

Perspective

- Health care system?
- Society?
- Patient?

- What difference might each make?

Duration required

- Must be long enough for all differences in cost and consequences between the programmes being considered to eventuate

- Treatment of hepatitis C

Time preference

- Do you have time preferences for costs and benefits?
- Need to bring all outcomes and costs to single time point to make them comparable
- Debates about differential rates
- Usually set by government
- UK now using 3.5% for both costs and benefits

Cost consequence analysis

ASIAN ANNALS

Original Article

Asian Cardiovascular & Thoracic Annals
0(0) 1–6
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DOI: 10.1177/0218492313491754
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SAGE

Staplers versus hand-sewing for pulmonary lobectomy: randomized controlled trial

Apichat Tantraworasin[1], Somcharean Seateang[1] and Nutchanart Bunchungmongkol[2]

Abstract

Background: division of the parenchymal lung for lobectomy is performed in patients who have an incomplete fissure. A stapler device can reduce postoperative air leak, but it is expensive.

Objective: to investigate the advantage of using a stapler, in terms of postoperative air leak and cost, compared to hand-sewn techniques.

Method: a non-blinded randomized controlled trial was conducted in Chiang Mai University Hospital, Thailand, from November 15, 2011 to September 30, 2012. Fifty-three adult patients were randomized to undergo a hand-sewn technique (27 patients) or stapler closure (26 patients).

Results: postoperative air leak in the stapler group was less than that in the hand-sewn group (7.7% vs. 29.6%, $p = 0.044$), and the duration of air leak in the stapler group was significantly shorter than that in the hand-sewn group (1.0 vs. 13.4 days, $p = 0.032$). The cost of treatment was not significantly different between groups; however, the total cost in the stapler group was less than that in the hand-sewn group (mean difference 4454 Thai baht (US$144.75).

Conclusion: a stapler reduces postoperative air leaks and the duration of air leaks. Furthermore, the total cost of treatment was comparable. Therefore, using staples may provide substantial financial benefits.

Keywords

Cost-consequence analysis, Lung neoplasms, Lobectomy, Surgical stapling

Cost consequence analysis

Consequence	Costs
Air leak less in stapler group 7.7% vs 29.6% (difference 21.9%) Air leak duration shorter in stapler group 1.0 vs 13.4 days	Technology costs B10,630 vs B1,022 (difference B9,608) Direct medical costs B24,470 vs B23,277 Total costs B109,057 vs B105,079 (difference B3,978)

Cost minimisation

- Assumes that there is NO DIFFERENCE in the benefits between two options
- So comparison driven by differences in costs

Cost effectiveness analysis

- Complete economic evaluation – relates differences in outcome to differences in costs
- Outcome according to the condition of interest e.g.
  - case of cancer
  - mmHg
  - facture prevented
- Difference with CC and CM is that costs are *related to outcome*

The NEW ENGLAND JOURNAL of MEDICINE

What Do We Gain from the Sixth Stool Guaiac?

Duncan Neuhauser, Ph.D., and Ann M. Lewicki, M.D.

N Engl J Med 1975; 293:226-228 | July 31, 1975 | DOI: 10.1056/NEJM197507312930504

Abstract The six sequential stool guaiac protocol has been advocated for screening of colonic cancer. Analysis of the expenditures involved in such a program shows that the cost of detecting cancer rises exponentially so that the marginal cost of the sixth test may be 20,000 times the average cost. The marginal cost is decreased with lower test sensitivity and increased with lower prevalence of colonic cancer. This result shows that even an inexpensive test can become quite costly in terms of cases detected. The marginal cost per case detected depends on the prevalence of the condition in the population screened and the sensitivity of the test applied. (N Engl J Med 293:226-228, 1975)

This is a great example which demonstrates

(a) Use of a “natural unit” of outcome in CEA

(b) Applicability of CEA to tests

(c) Importance of <u>incremental</u> analysis

(Additional cost per additional benefit)

- Assuming independence in tests, we can reduce total false negatives by repeating test i.e. pick up cases missed with initial testing

- Sensitivity of guaiac test = 11/12

- Population = 10,000 people

Diminishing returns

N Tests	N cases detected	False negatives
1	0.9166666	1 in 12
2	0.9130555	1 in 144
3	0.9994213	1 in 1,728
4	0.9999517	1 in 20,736
5	0.9999959	1 in 248,832
6	0.9999996	1 in 2,985,984

Cost per additional case detected (1)

Tests	Cancers detected by **this many** tests	Total cost of this many tests	Cost per detection
0	0	$0	---
1	66	$77,550	$1,175
2	71.5	$107,756	$1,507
3	71.9583	$130,283	$1,811
4	71.9965	$148,217	$2,059
5	71.9997	$163,255	$2,267
6	72	$175,749	$2,441
			3rd column entry divided by the 2nd column entry

Cost per additional case detected (2)

Tests	Cancers detected by **this** test	Marginal cost of **this** test	Marginal cost per detection
0	0	---	---
1	66	$77,550	$1,175
2	5.5	$30,206	$5,492
3	0.458	$22,527	$49,150
4	0.038	$17,934	$469,545
5	0.003	$15,038	$4,724,666
6	0.0003	$12,494	$47,104,652
			3rd column divided by 2nd column

- Average costs and outcomes is not useful
- Incremental cost effectiveness ratio indicates the economic efficiency of the technology

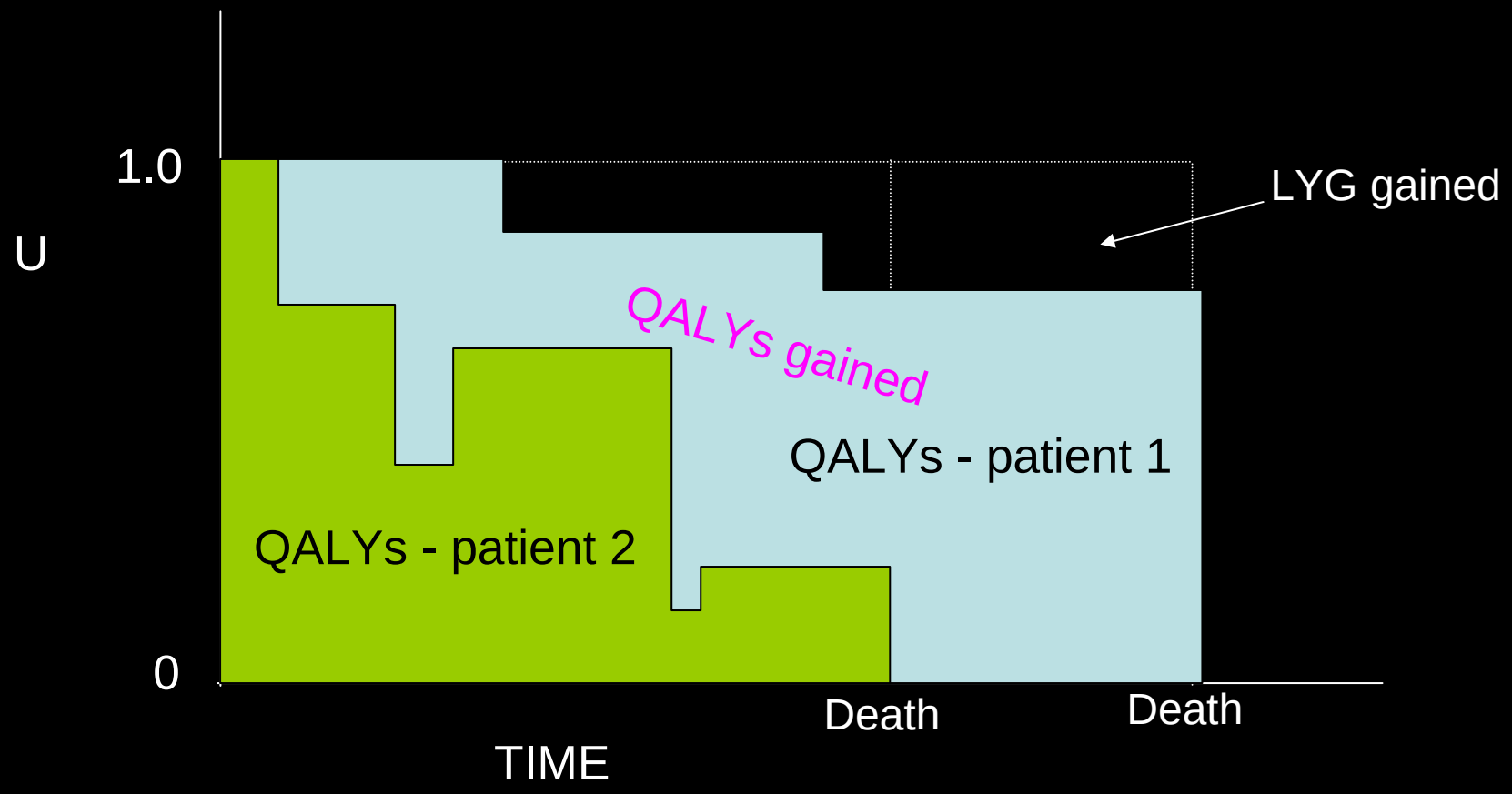
Cost per QALY (Cost Utility)

- Outcome is the Qualty Adjusted Life Year
- Preferred in many jurisdictions
- Combines mortality and morbidity into a single outcome
- ***Allows comparison between different programmes***
- How much is society willing to pay?
  - **THIS SETS THE THRESHOLD FOR ACCEPTING A TECHNOLOGY**

Measuring the Q in QALYs

- Utility – bounded negative infinity and 1.0
- Death = 0
- Perfect health = 1.0
- So 0.5 = time spent is “worth” half as much as being in perfect health
- Negative states mean you’d rather be dead

QALY gains - example



How to get the quality weight

- Preference based approaches preferred on basis of economic theory
  - Standard Gamble
  - Time Trade Off
  - Person Trade Off
  - Visual Analogue Scale

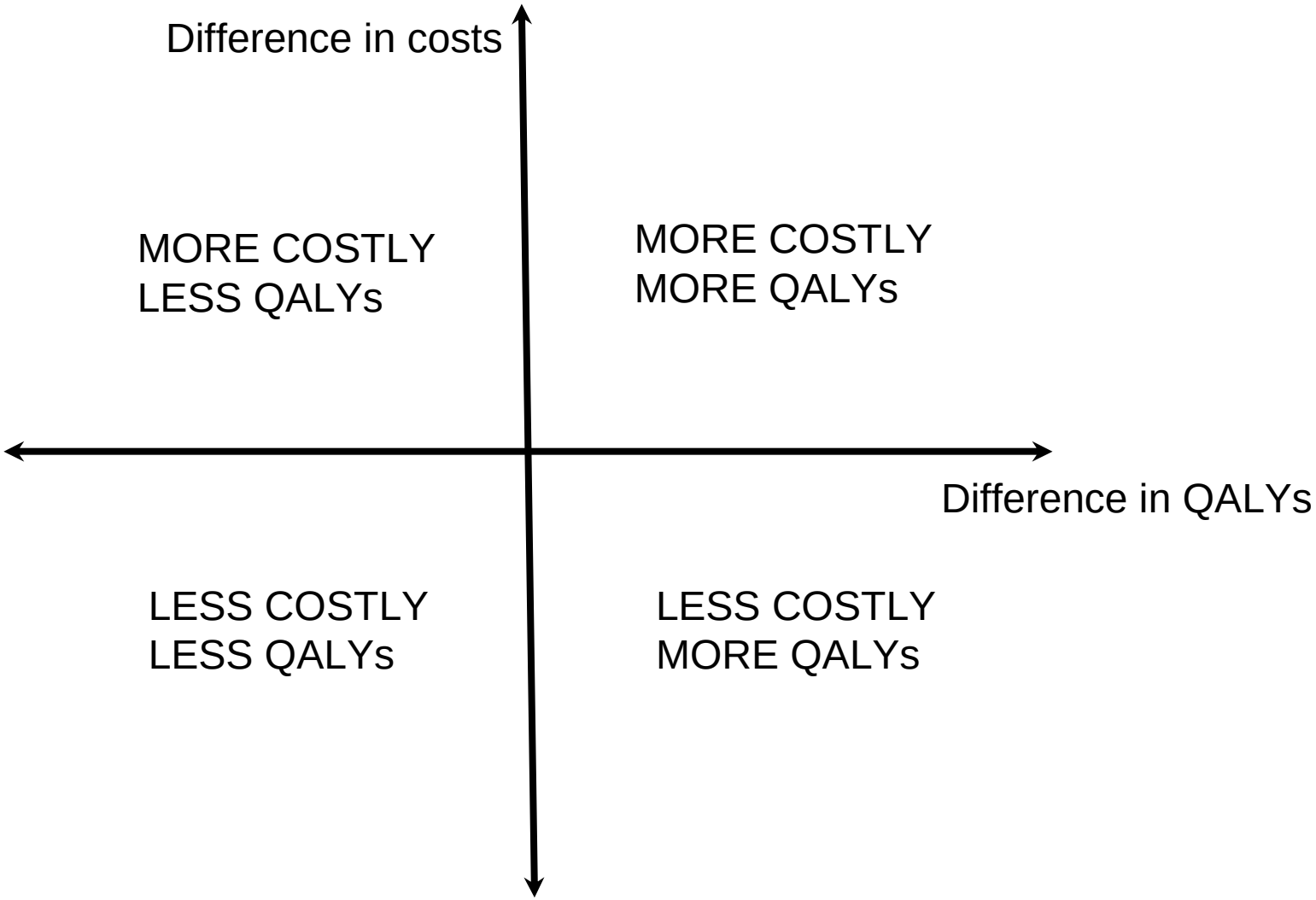
Standard gamble

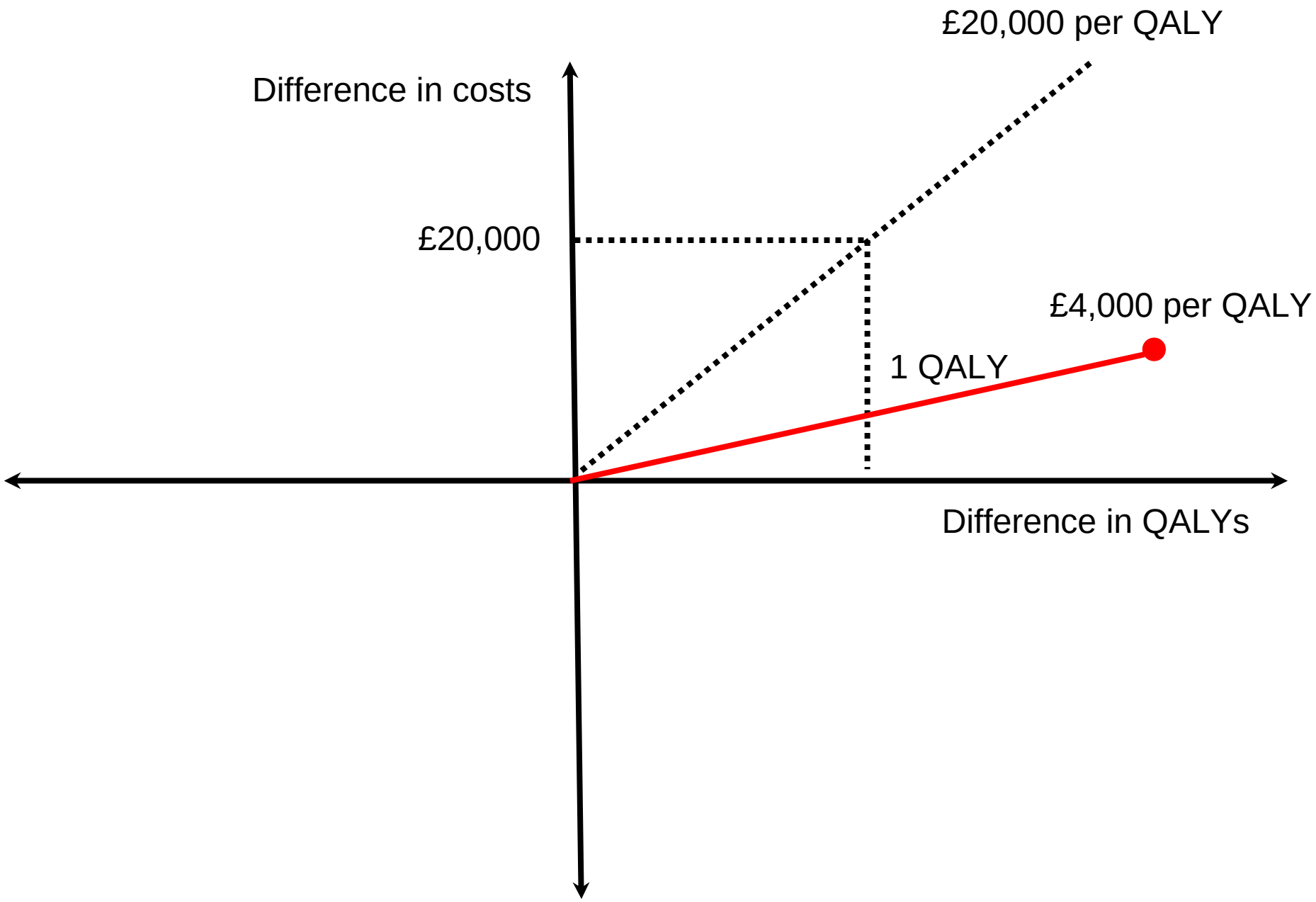
- You are in some state of health (actual or imagined)
- Imagine I could offer you a treatment with
  - A probability (p) of completely curing you
  - A probability (1-p) of killing you immediately
- I then offer you the choice of
  - Staying as you are for a long time
  - Taking the risky treatment
  - At a range of values for p
- The point at which you are indifferent between choice or staying as you are indicates how bad you think the state is

Time Trade Off

- Again, imagine being in a health state
- How much of your existing life expectancy in the health state of interest would you trade for a shorter period in perfect health?
- If you would trade 30% of your life expectancy, then your current state has a utility weight of 0.7

The cost effectiveness plane



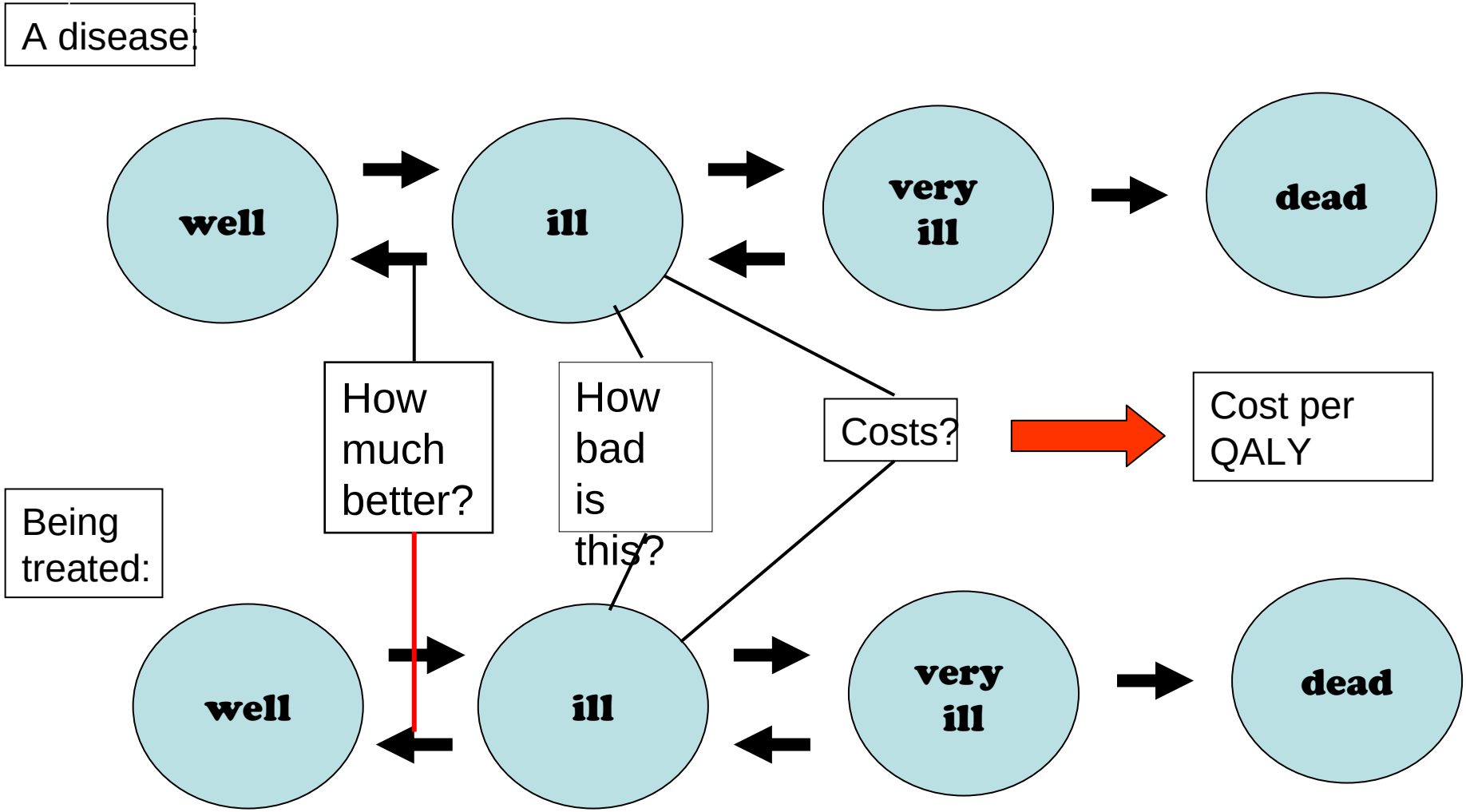

£20,000 per QALY
Difference in costs
£20,000
£4,000 per QALY
1 QALY
Difference in QALYs

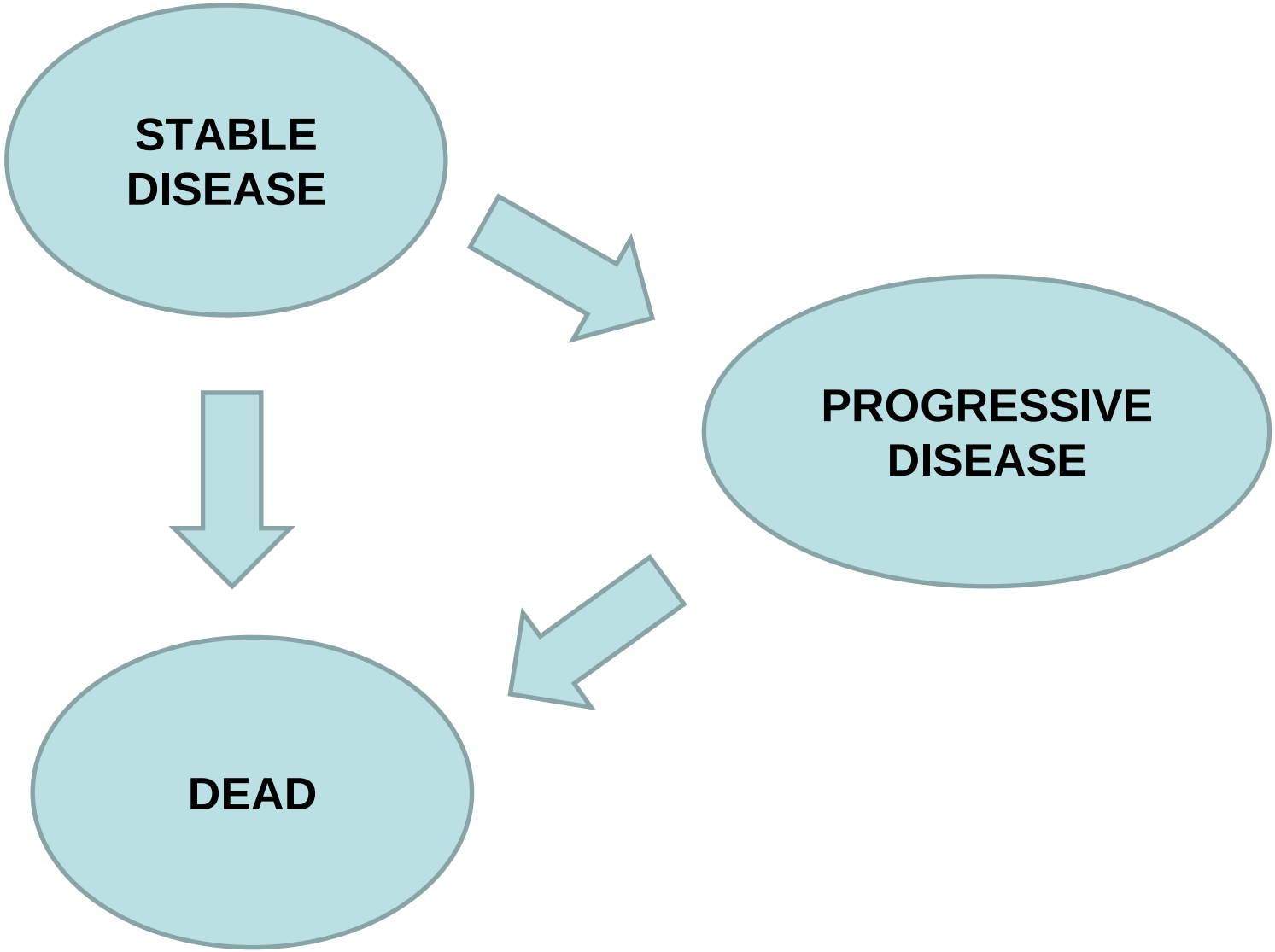
Pause ☺

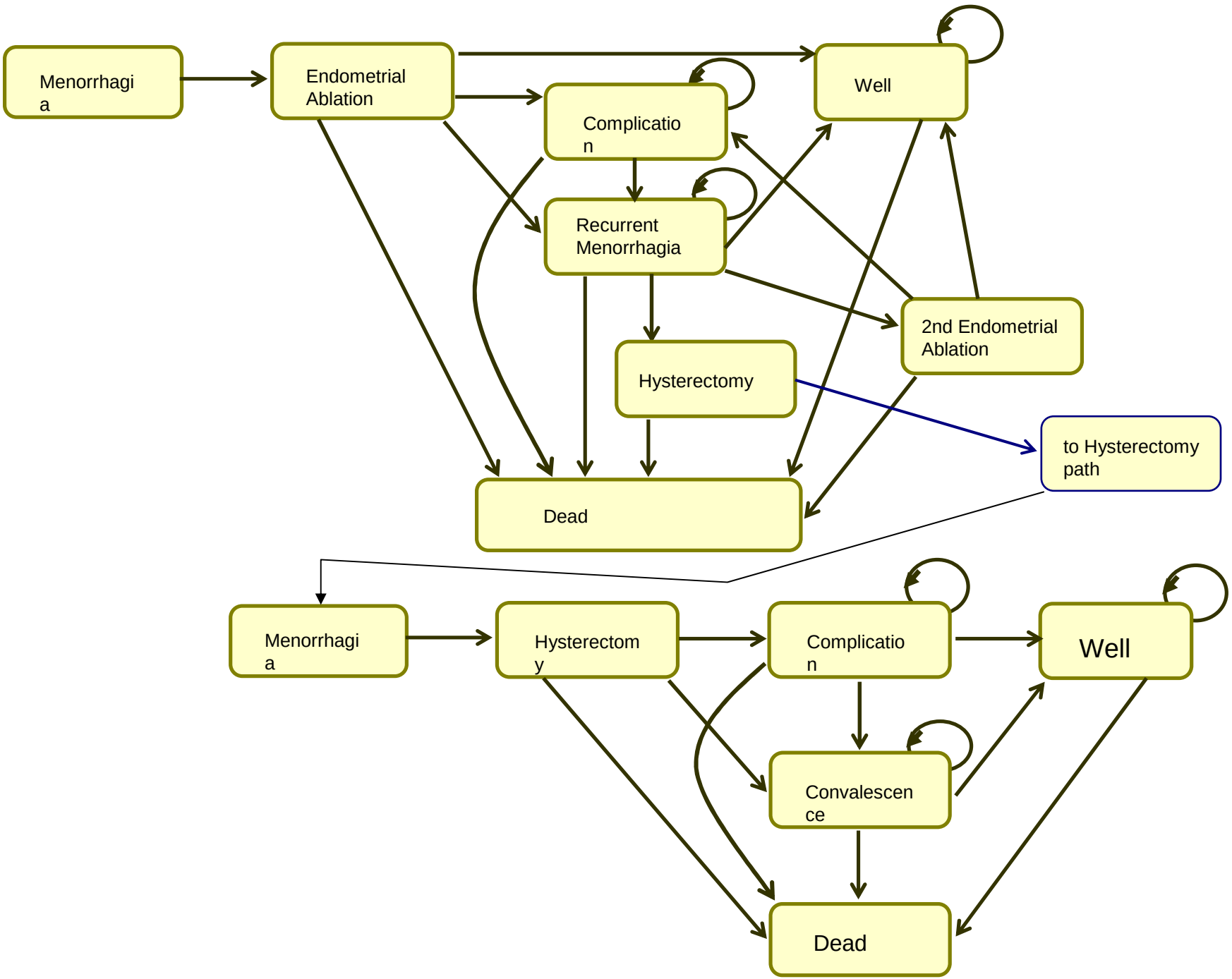
Modelling in HTA

- Often health state transition models
- Markov (assumes no memory) most common
- Within trial analyses may yield cost per QALY but usually too short to satisfy policy needs for economic evaluation
- Models may be “bolted on” to the end of trials to model the long term

Markov (state-transition) Model




STABLE DISEASE
PROGRESSIVE DISEASE
DEAD

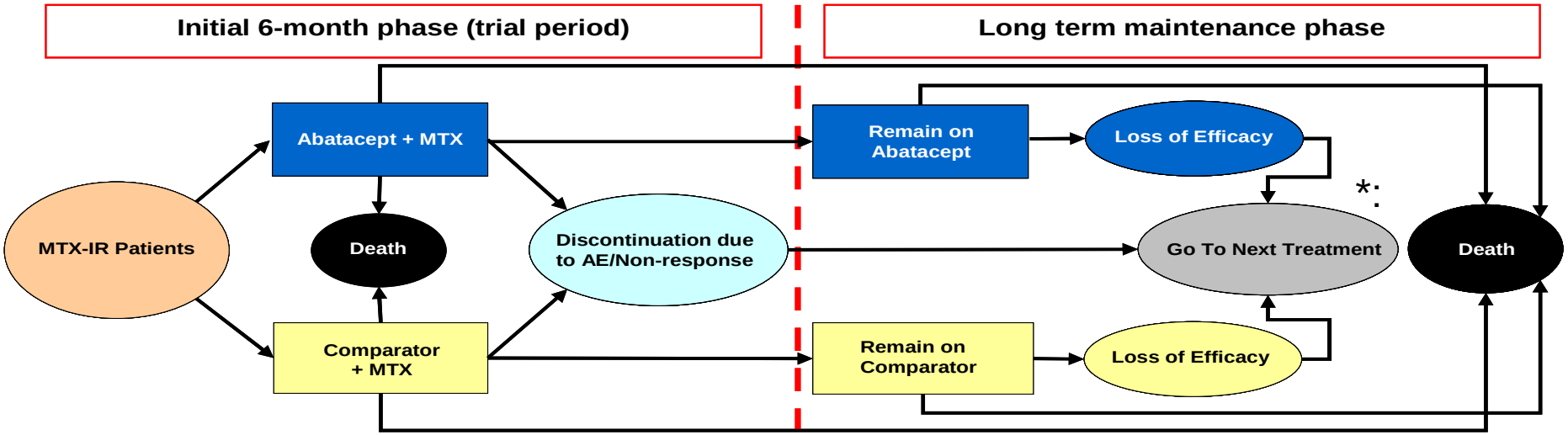

Menorrhagia
Endometrial Ablation
Well
Complication
Recurrent Menorrhagia
2nd Endometrial Ablation
Hysterectomy
to Hysterectomy path
Dead
Menorrhagia
Hysterectomy
Complication
Well
Convalescence
Dead

Cost effectiveness: model structure

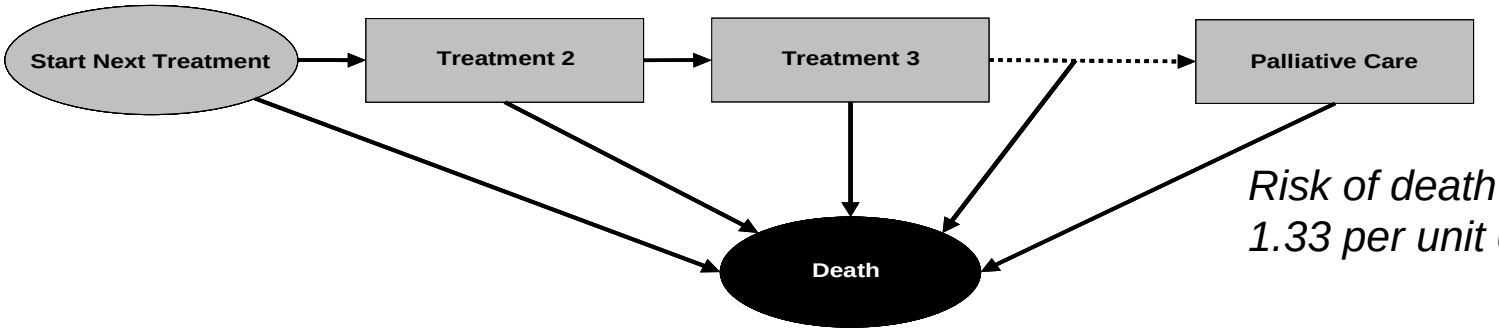
Mean HAQ change from baseline from MTC

Response defined as 0.3 improvement

Average duration = 4.21 years for all biologic treatments



*DMARDs:



Risk of death increases by 1.33 per unit of HAQ

Uncertainty

- Structural
  - The way the problem is characterised (types of health state, duration of analysis)
- Methodological
  - Potential for bias arising from the methods used to inform parameterisation of the model
- Parameter
  - Variation within possible parameter inputs

Inputs

- EFFECTIVENESS
  - Comparisons
  - Time horizon
- COSTS
  - Amount
  - Value
  - Perspective
- BENEFITS
  - What value?

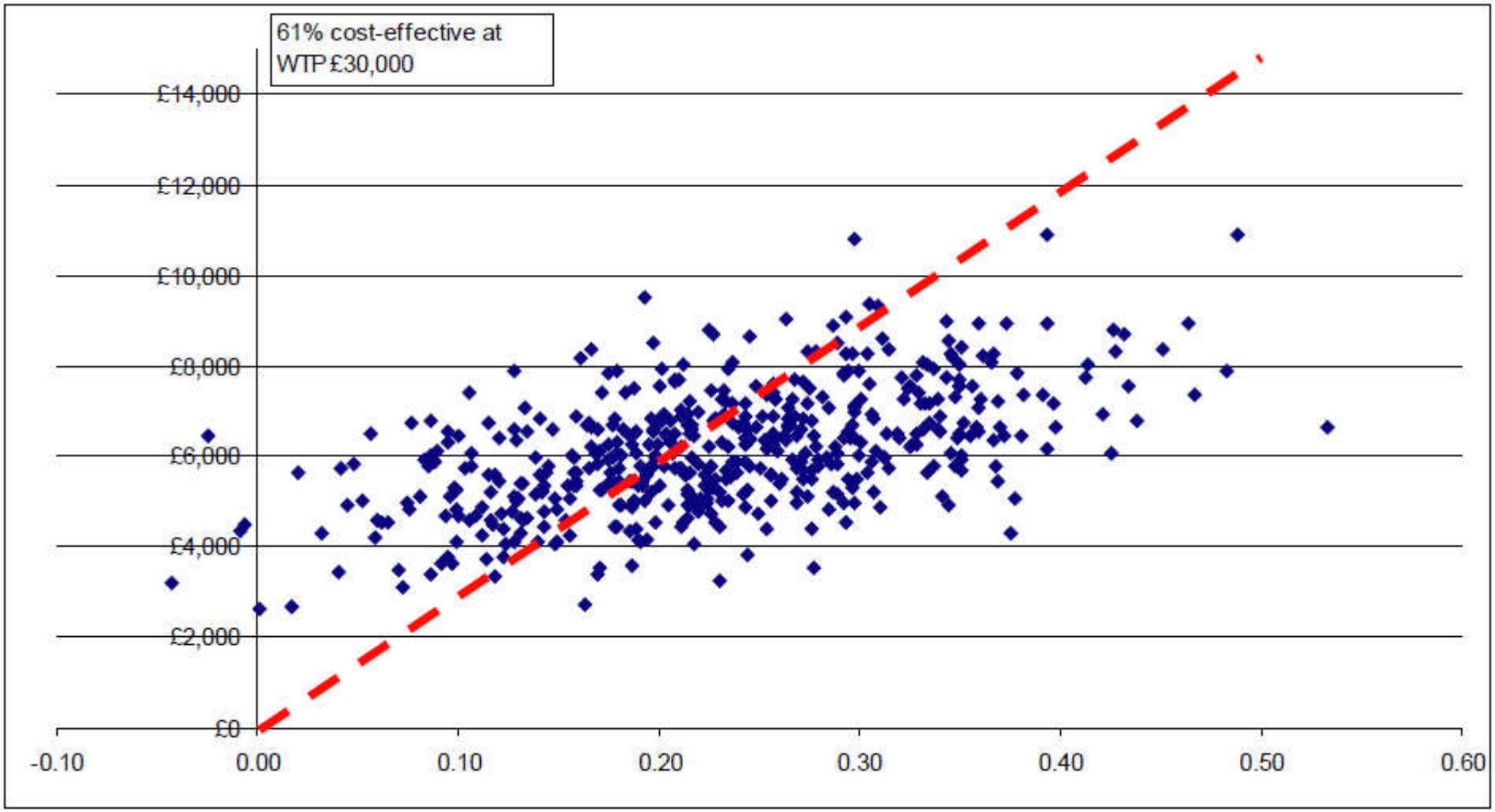
Uncertainty – structural and univariate parameter

Alternative analyses			Impact on incremental results			
			Infliximab			
Parameters	**Base-case**	**Variation**	**Costs £**	**QALYs**	**ICER (£/QALY)**	**% change**
Base-case	-	-	5,434	0.21	25,355	-
Discount rate effects and costs	3.5%	0% both	8,532	0.33	25,674	1.26%
		1.5% effects and 6% for costs	5,731	0.16	36,065	42.24%
		6% both	4,792	0.18	27,014	6.54%
Analysis time frame	Life time	5 years	3,044	0.06	49,012	93.30%
Utilities	Hurst	Bansback	6,051	0.25	24,390	3.80%
HAQ response rate	0.3	0.22	5,675	0.21	26,884	6.03%
Vial wastage infliximab	Yes	No	10,078	0.17	57,843	128.13%
Dose increase infliximab	Yes	No	9,642	0.26	37,025	46.02%

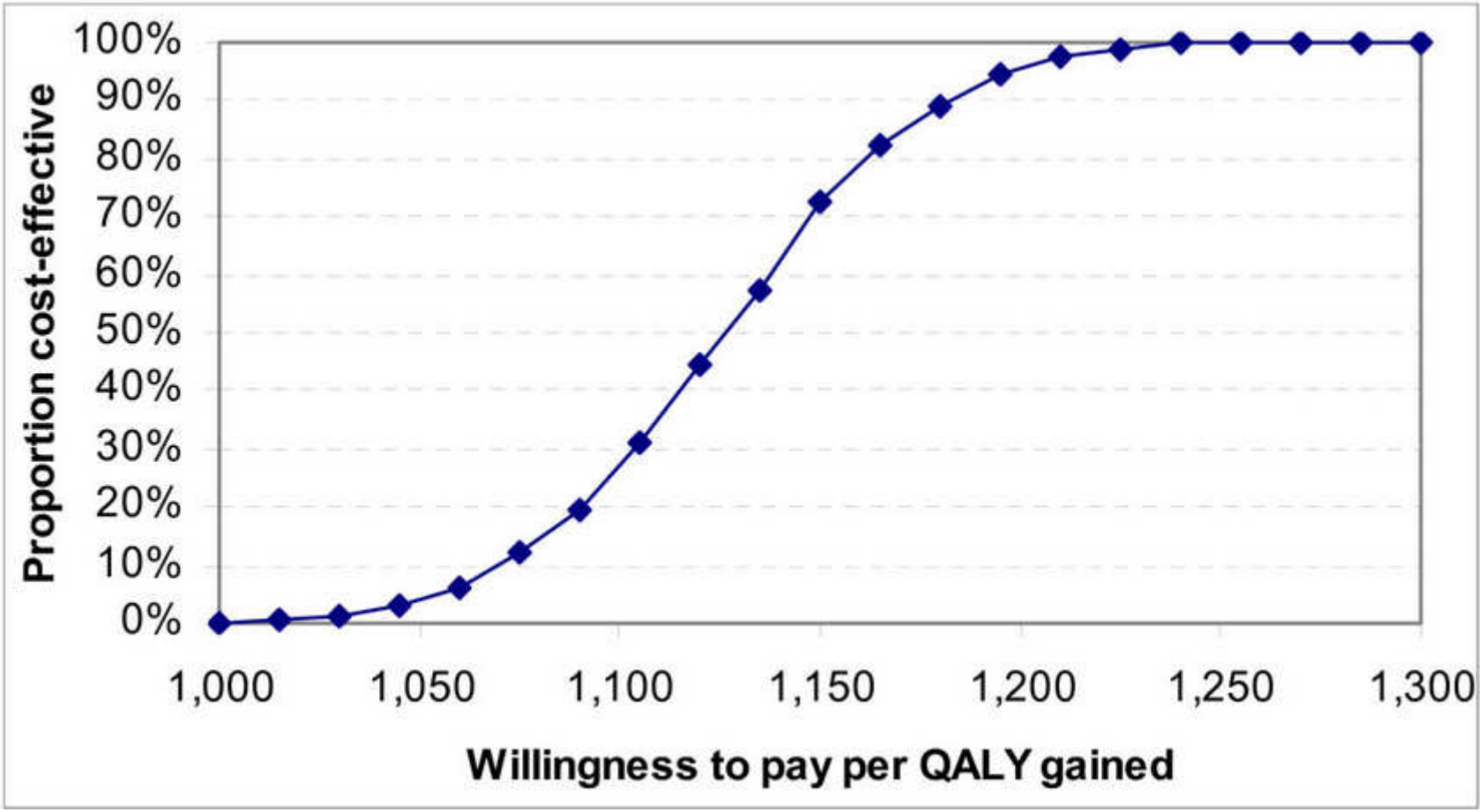
But parameter values are not certain

- Confidence intervals for a treatment effect
- Variation in mean cost between populations
- Health state values vary by
  - Methods, respondents, instrument
- So we can run and re-run models, picking up different values for parameters from different distributions
- Then look at the population of ICERs

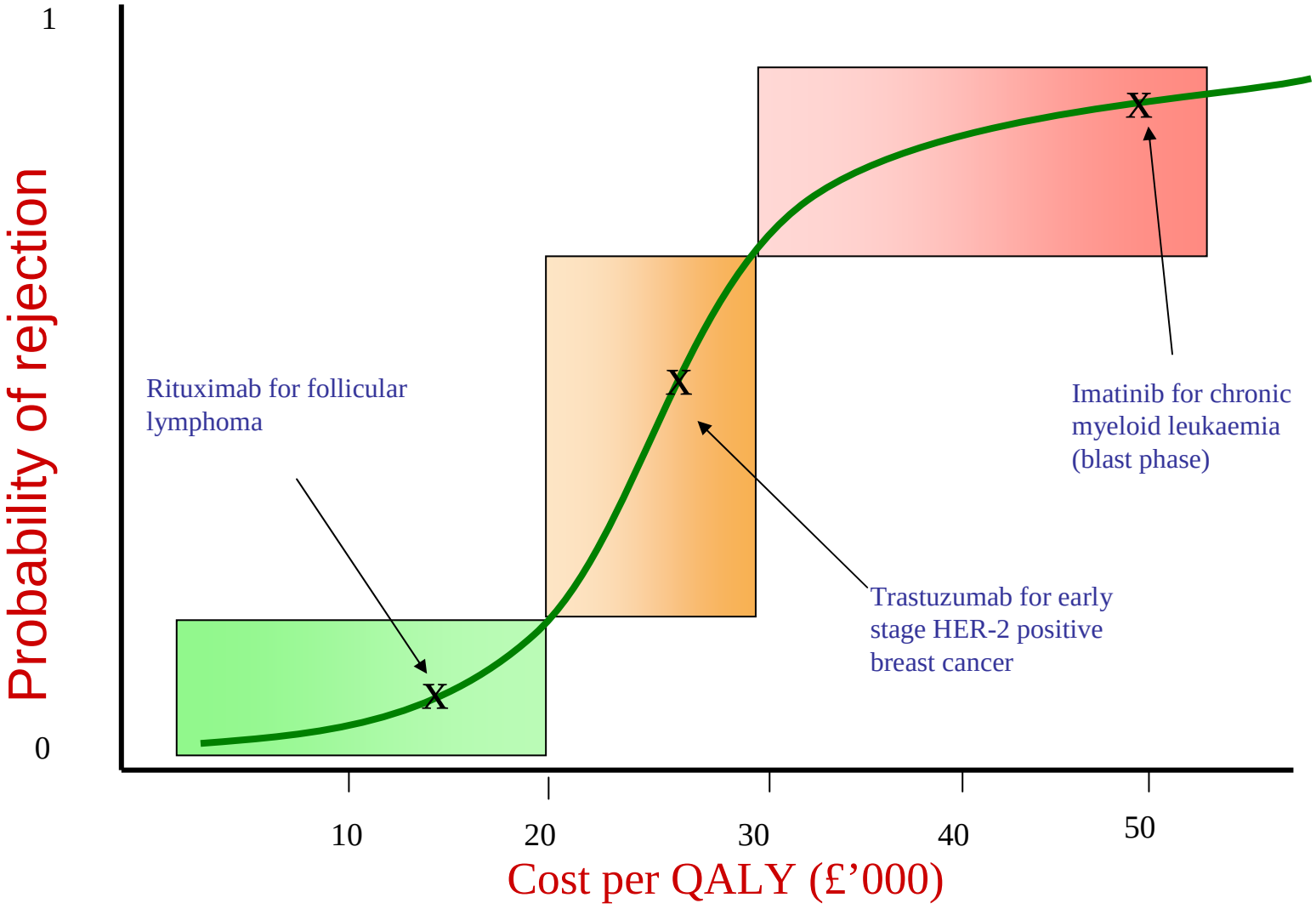
Uncertainty - PSA



Cost effectiveness acceptability curve



NICE cost-effectiveness threshold



NICE International

Another pause ☺

Further issues

- Special circumstances and appraisal decisions
- End of Life criteria
- Patient Access Schemes
- Budget Impact Analysis

Application of ‘special circumstances’

Table 1

Application of ‘special circumstances’ in the appraisal of some products with incremental cost-effectiveness above £30 000 per quality adjusted life year

Topic	ICER (‘000s)	Severity	End of life*	Stakeholder persuasion	Significant innovation	Disadvantaged population	Children
Riluzole (motor neurone disease)	38–42	✓	✓	✓			
Trastuzumab (advanced breast cancer)	37.5	✓			✓		
Imatinib (chronic myeloid leukaemia)	36–65	✓			✓		
Imatinib (gastrointestinal stromal tumour)		✓	✓		✓		
Pemetrexed (malignant mesothelioma)	34.5	✓	✓			✓	
Ranizumab (age-related macular degeneration)	>>30			✓	✓		
Omalizumab (severe asthma)	>30	✓		✓	✓		
Sunitinib (advanced renal cancer)	50	✓	✓	✓	✓		
Lenalidomide (multiple myeloma)	43	✓	✓		✓		
Somatotropin (growth hormone deficiency)	n/a			✓	✓		✓
Chronic subcutaneous insulin infusion (childhood Type 1 diabetes)	n/a			✓			✓

*End-of-life considerations have only been explicitly taken into account since January 2009 on the basis of supplementary advice from the Institute to the Appraisals Committee.
ICER, incremental cost-effectiveness ratio (£ per quality-adjusted life year).

Rawlins, Barnett, Stevens Br J Clin Pharmacol 2010

Appraising life-extending, end of life treatments 2009 Supplementary Advice

- The treatment is indicated for patients with a short life expectancy, normally less than 24 months and;
- 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, and;
- The treatment is licensed or otherwise indicated, for small patient populations.
- Plus
  - Estimates of extensions to life are robust …
  - Assumptions in the economic model are plausible and robust

Some were happy…

- “This is a most welcome move. It is not tolerable for patients in other countries to have standards of care which are higher than those in England/Wales, especially when the nature of the illness is life limiting.” *Patient*

- “We would like to congratulate NICE for proposing this scheme which we feel has the potential to make a significant difference to the way in which new treatments for patients nearing the end of life are appraised.” *Pharmaceutical industry*

…and others were not.

- “I believe that all claimants on NHS resources should be treated the same, regardless of the nature and cause of their health problem. For the first ten years of its life, this was the Institute’s position…There was little point spending so much effort establishing your reputation for independence and robustness, only to roll over now.

- The claim that those terminally ill value life highly is correct, but do not those with deteriorating sight value their continuing ability to see, those with mental health problems value their ability to maintain their mental functioning, those with pain from chronic disease value a pain-free state, just as highly? Others who depend on the NHS will pay the opportunity costs of extra funding for cancer drugs, and the equity of the service will be damaged.” *NHS professional*

Patient Access Schemes

"Patient access schemes are proposed by pharmaceutical company and agreed by DH to improve the cost effectiveness of a drug and enable patients to receive access to cost effective innovative medicines"

- *The Pharmaceutical Price Regulation Scheme 2009 between DH and the ABPI*

Budget impact to assist implementation…

Budget impact …

…estimates the impact on annual healthcare use and cost for the first, second and subsequent years after the introduction of the new product for a population *(Mauskopf, JA et al. 2005)*

… and helps estimate the cost of implementation

Economic evaluation (cost-effectiveness analysis)…

.. the comparative analysis of alternative courses of action in terms of both their costs and consequences. *(Drummond et al. 1987)*

… and helps determine what is cost-effective and to be recommended

Practical session

- The standard gamble
- Method for assessing the value associated with a health state
- One method of obtaining QALY weighting

Getting Utilites

- Description of HS health states to experts for opinion (0.95)
- Eliciting utilities sufferers
  - Visual analogue scale
  - Time trade off (0.67)
  - Standard Gamble
- Mapping onto health state measures for which preferences are known e.g. EQ5D
  - Mobility
  - Self-care
  - Usual activity (0.85)
  - Pain / discomfort
  - Anxiety / depression
- Getting scenarios valued by members of the public

PS - these are the real values for utilities associated with impotence used in an evaluation of the cost utility of viagra

Health State Description

- Moderate to severe pain in a wide range of sites
- Moderate invountary and sometimes painful contractions of muscles throughout the body
- Moderate to severe stiffness or tightness of the muscles which may interfere with movement, speech or manner of walking
- Moderate tremor (shaking in the upper limbs/head)
- Moderate bladder problems such as incontinence
- Slight sleep disturbance

Standard gamble

- Imagine you are in this state
- You have a series of pairs of choices
  - A:
    - Remain in this state for 10 years until you die
- OR
  - B:
    - Take a gamble between full health now or death now (like a sometimes-magic bullet) …

A:
Stay as you are for 10 yrs then die

- Or B: take a gamble….
  - 100% chance of full health for 10 years then die
  - 95% chance of full health, 5% chance of death now
  - 90% chance of full health, 10% chance of death now
  - 85% chance of full health, 15% chance of death now
  - 80% chance of full health, 20% chance of death now
  - 75% chance of full health, 25% chance of death now
  - 70% chance of full health, 30% chance of death now
  - 65% chance of full health, 35% chance of death now
  - 60% chance of full health, 40% chance of death now
  - 55% chance of full health, 45% chance of death now
  - 50% chance of full health, 50% chance of death now

A:
Stay as you are for 10 years then die

- Or B: take a gamble:
  - 45% chance of full health, 55% chance of death now
  - 40% chance of full health, 60% chance of death now
  - 35% chance of full health, 65% chance of death now
  - 30% chance of full health, 70% chance of death now
  - 25% chance of full health, 75% chance of death now
  - 20% chance of full health, 80% chance of death now
  - 15% chance of full health, 85% chance of death now
  - 10% chance of full health, 90% chance of death now
  - 5% chance of full health, 95% chance of death now
  - 100% chance of death now

Some utilities to ponder

• Hemiparesis, non-dominant side	0.50
• Hemiparesis, dominant side	0.36
• Independent but not recovered	0.71
• Rankin 2-3	0.71
• Rankin 2-3	0.90
• Rankin 2	0.59
• Menorrhagia	0.56