Theory and principles of cost-effectiveness analysis

Karl Claxton

5/2/2020

THE UNIVERSITY of York

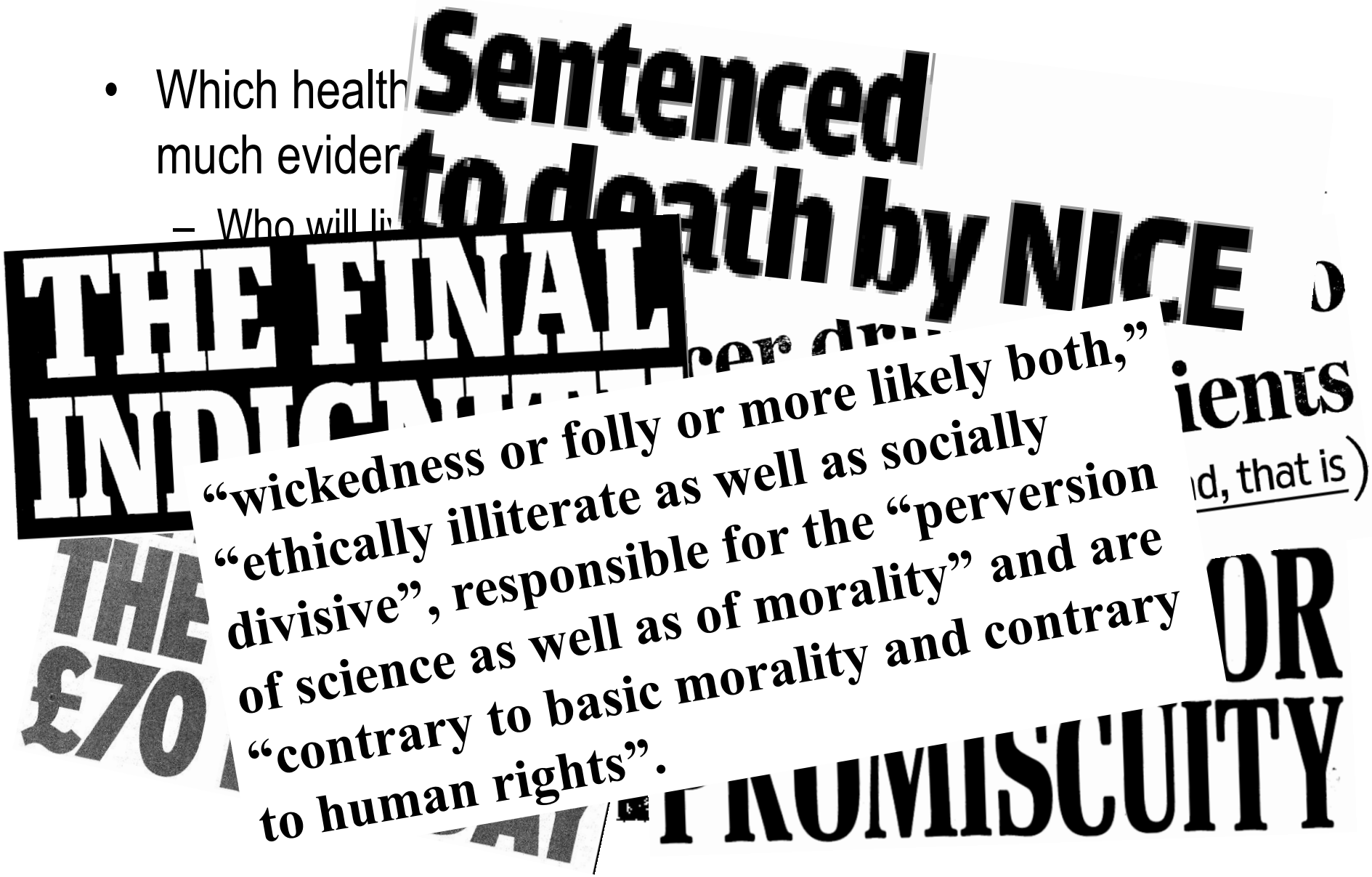
CHE
Centre For Health Economics

Overview

- Some normative foundations
- Making decisions
- Multiple alternatives
- Which cost effectiveness threshold?
- What perspective?
- Non mutually excusive alternatives
- Taking account of the timing of costs and benefits
- Why does uncertainty matter?

Social choice in health

- Which health
  much evider
  - Who will li



What is the social good?

- What is social welfare?
  - Vector of individual welfare (w^i)

    $W = (w^1, .., w^i, .., w^I)$
  - But how is w^i to be defined and measured?
- From welfare to utility?
  - Individual is the best/only judge of w^i
  - Individuals behave to maximise w^i
    - if x preferred to y then w^i is greater with x than y
    - individual preference (utility) is the measure of welfare
    - Can infer welfare from individual choices (in markets)
- Some implications
  - U^i represents ordinal preferences of i (cant say how much more or less)
  - Utility is not unit comparable (cant compare peoples utility)
  - Utility (preference) is the only admissible information
  - No comment on the source of preference

Central tenets of 'Welfarism'

- Utility principle
  - Individuals rationally maximise their welfare (order and choose options)
- Individual sovereignty
  - Individual is the best/only judge of welfare
- Consequentialism
  - Not processes, intentions or sources of preference
- Welfarism
  - Judging the goodness of states only by individual utility (preference) information
  - Preference (utility and welfare) is revealed in markets and surogates
- Change in welfare?
  - Some better off no one worse off
  - Could (in principle) any losers be compensated by gainers?
  - Market prices indicate compensation required so reflect social value

Costs and benefits valued using market prices

- "...in situations where there are no externalities or public goods, no distorting taxes or monopolies, and where there are fully informed consumers, the competitive market acts as a giant (but decentralized) cost-benefit calculator. No second guessing by [health] economists is required." Pauly (1996), page 103

Some implications

- “Heath care programmes should be judged in the same way as any other proposed change: i.e., the only question is do they represent a potential Pareto improvement (as measured by individual utility) not do they improve health outcomes as measured in either physical units or health state utility [QALYs]. It is possible that a programme may increase the health of some but reduce the health of others. If those that gain health outcome can compensate those that lose health (measured by individual willingness to pay) then the programme may be a potential Pareto improvement even if the health outcomes overall are lower.” Mark Pauly, 1995.

Mark and Milton or Amartya

“Perfectly disgusting….A state can be Pareto optimal with some people in extreme misery and others rolling in luxury, so long as the miserable cannot be made better off without cutting into the luxury of the rich. Pareto can, like Ceasar’s spirit, come hot from hell” Sen

“Those that object to the market object to freedom itself” Friedman

So why not Mark and Milton?

- Current distribution isn't optimal
  - Can estimate for a particular distribution
  - Which distribution?
  - Adjust all compensation (including market prices)

- Market (shadow) prices don't represent social values
  - Don't except the narrow definition of welfare (utility information)
  - Don't believe in the nirvana of the neoclassical world
  - Not practical anyway (theory of second best etc)

If not the invisible fist?

- Specify explicit social welfare function
  - What and who counts?
  - What weights should be used?
  - How can any social welfare function claim legitimacy
    - Who should decide?
    - What process should be used?
- Maybe Freidman's got a point after all?
  - Paternalism at best
  - Lack of accountability and danger of dictatorship

Liberty or leviathan?

Legitimate institutions and process

- Accountable higher authority (principal)
  - Task of balancing competing claims, liberty and social justice
  - Devolves responsibility and resources to meet specific objectives
- Devolved authority (agent)
  - Asked to meet explicit (necessarily narrow) objectives
  - Given the resources to do the job
- Agent doesn't meet all the objectives of the principal
  - Impossibility of expressing an explicit social welfare function
  - Observe the implications of some latent but legitimate welfare function
- Modest claims based on implied social values
  - Legitimacy of any claim rest on the legitimacy of institutional arrangements

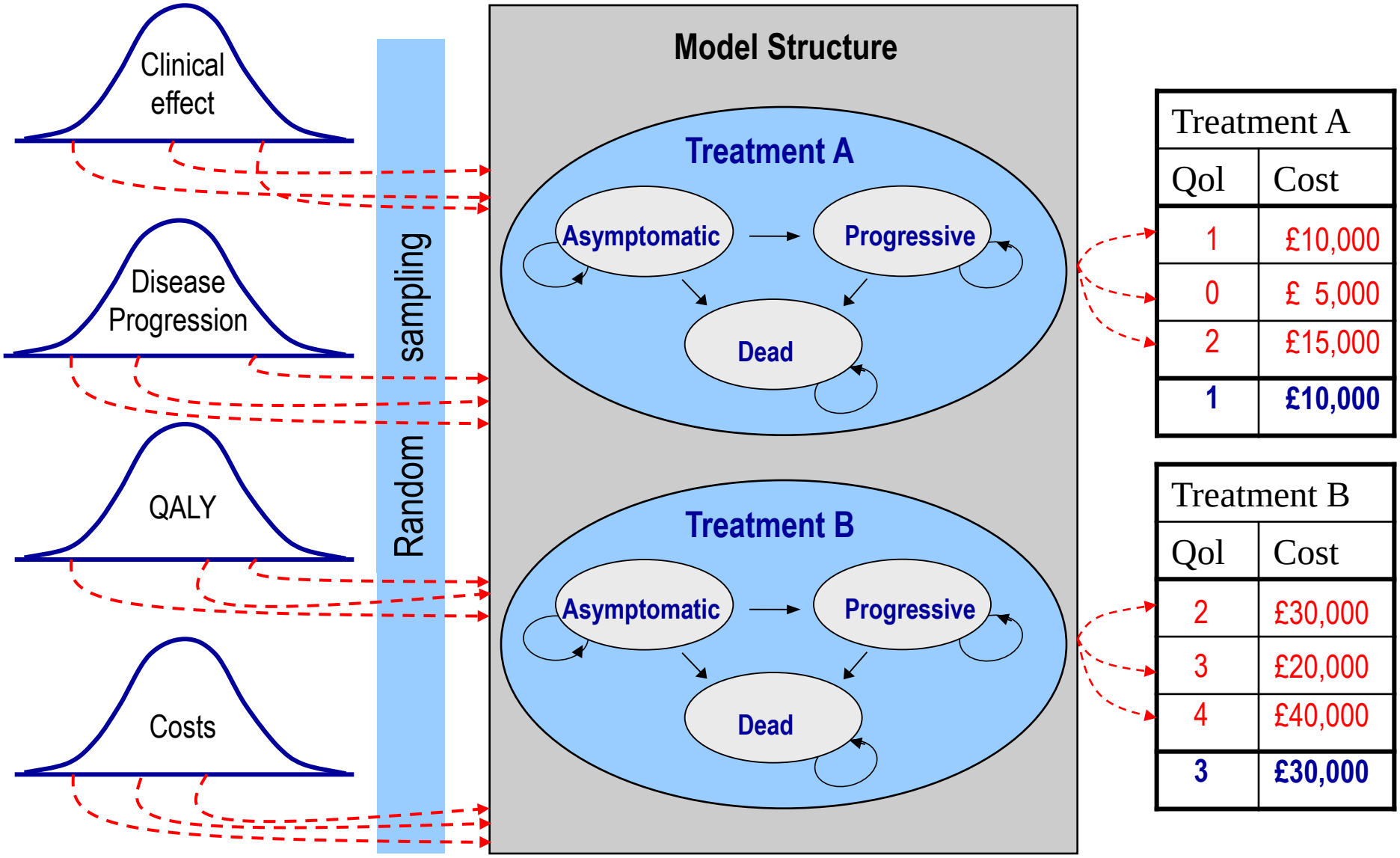
The role of economists?

"If economists could manage to get themselves thought of as humble, competent people, on a level with dentists, that would be splendid!" Keynes

Illegitimate institutions and you cant contribute to change?

You have no business being a dentist,
"pursue change through any other means necessary"

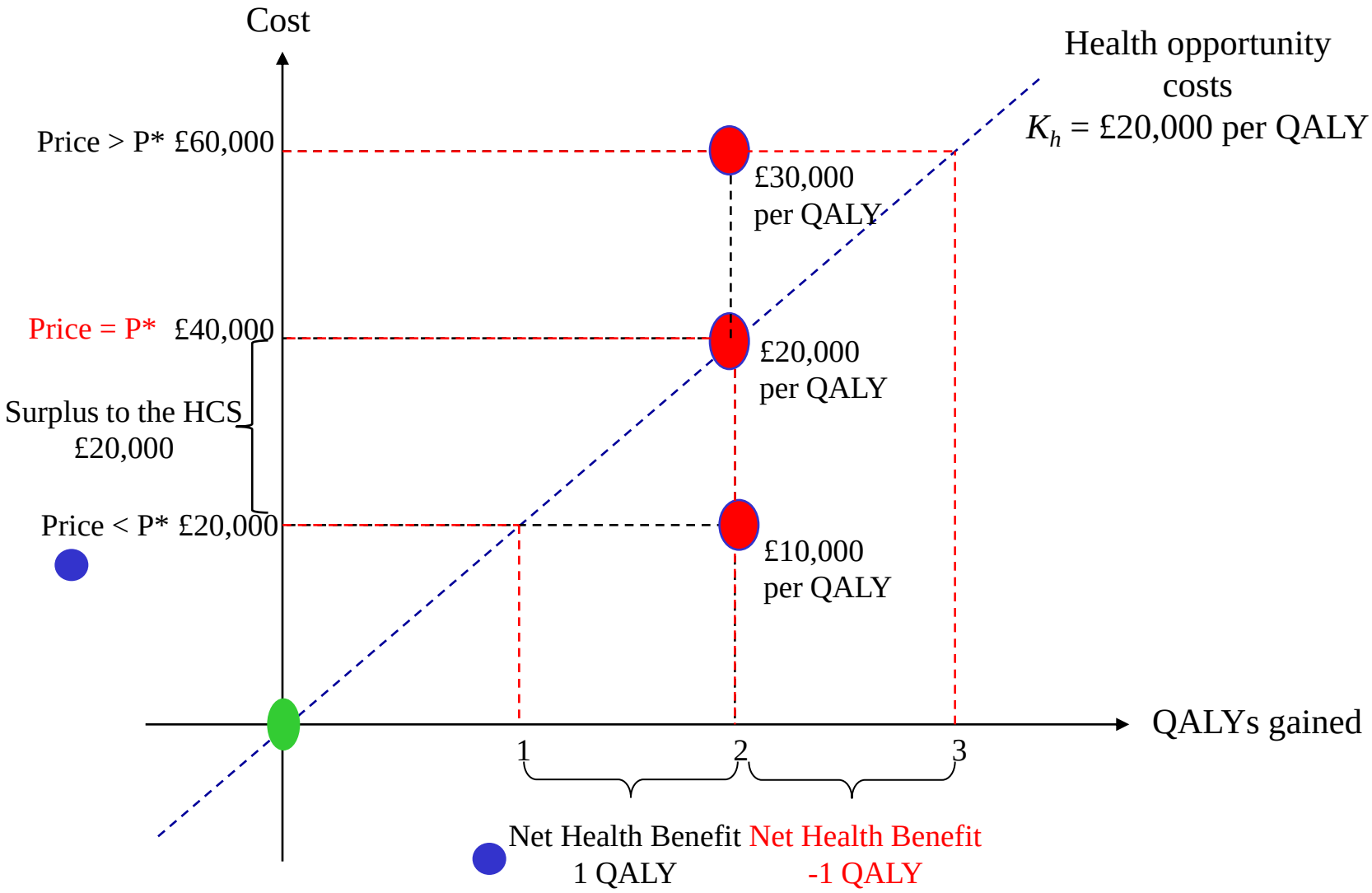
What do we need to know?



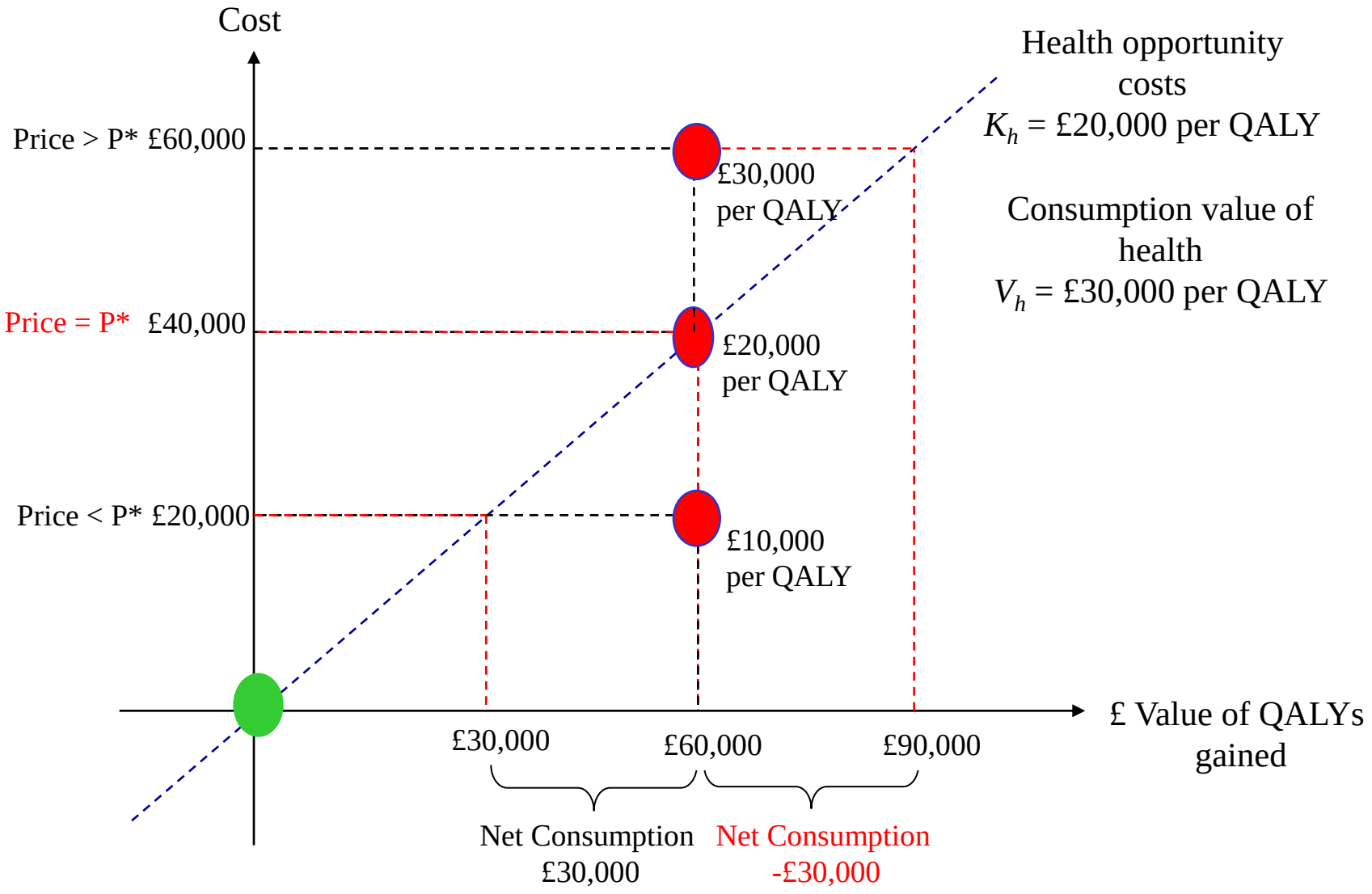
Treatment A	
Qol	Cost
1	£10,000
0	£ 5,000
2	£15,000
1	**£10,000**

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

Comparing benefits and costs?



What about willingness to pay?

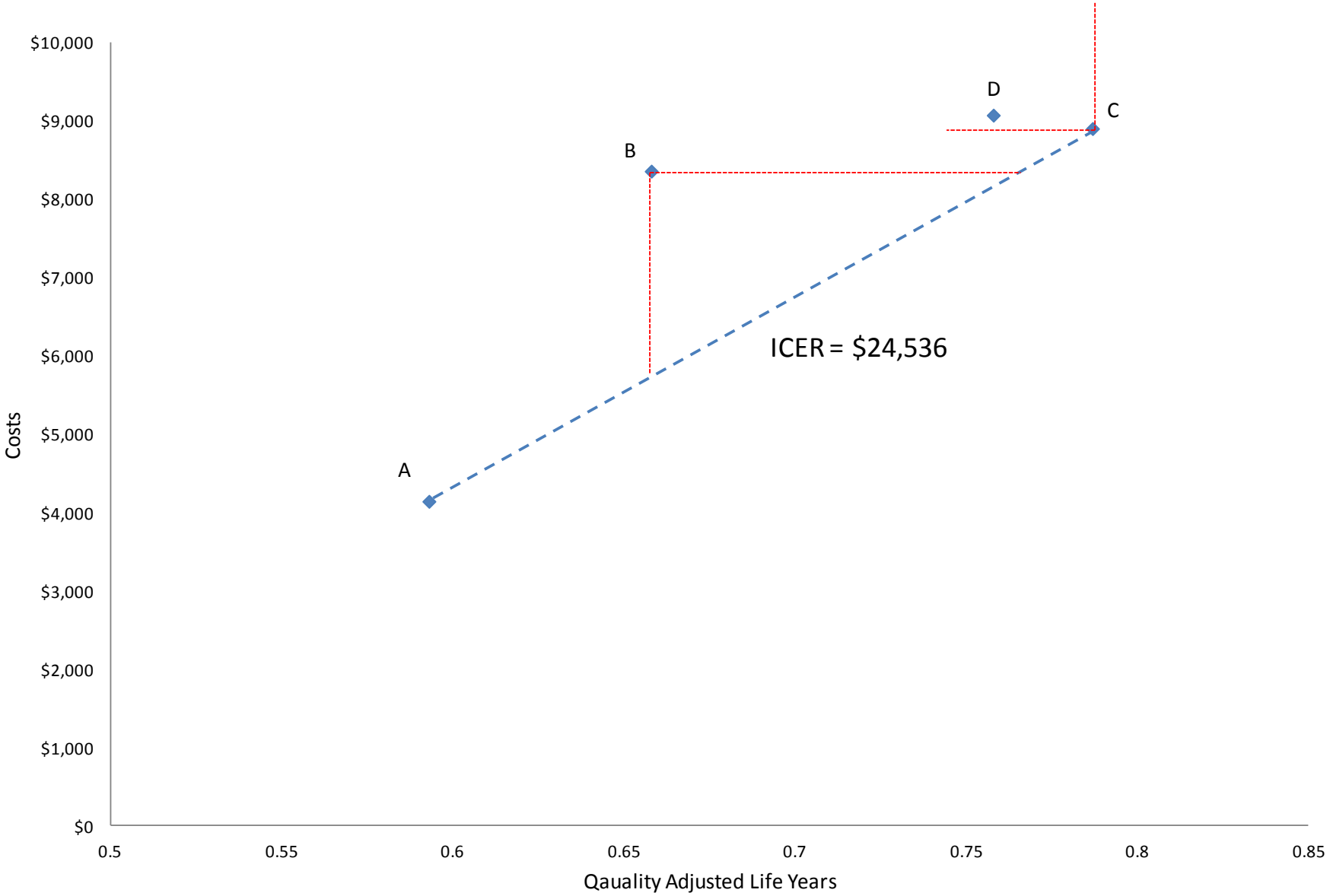


Comparing multiple alternatives

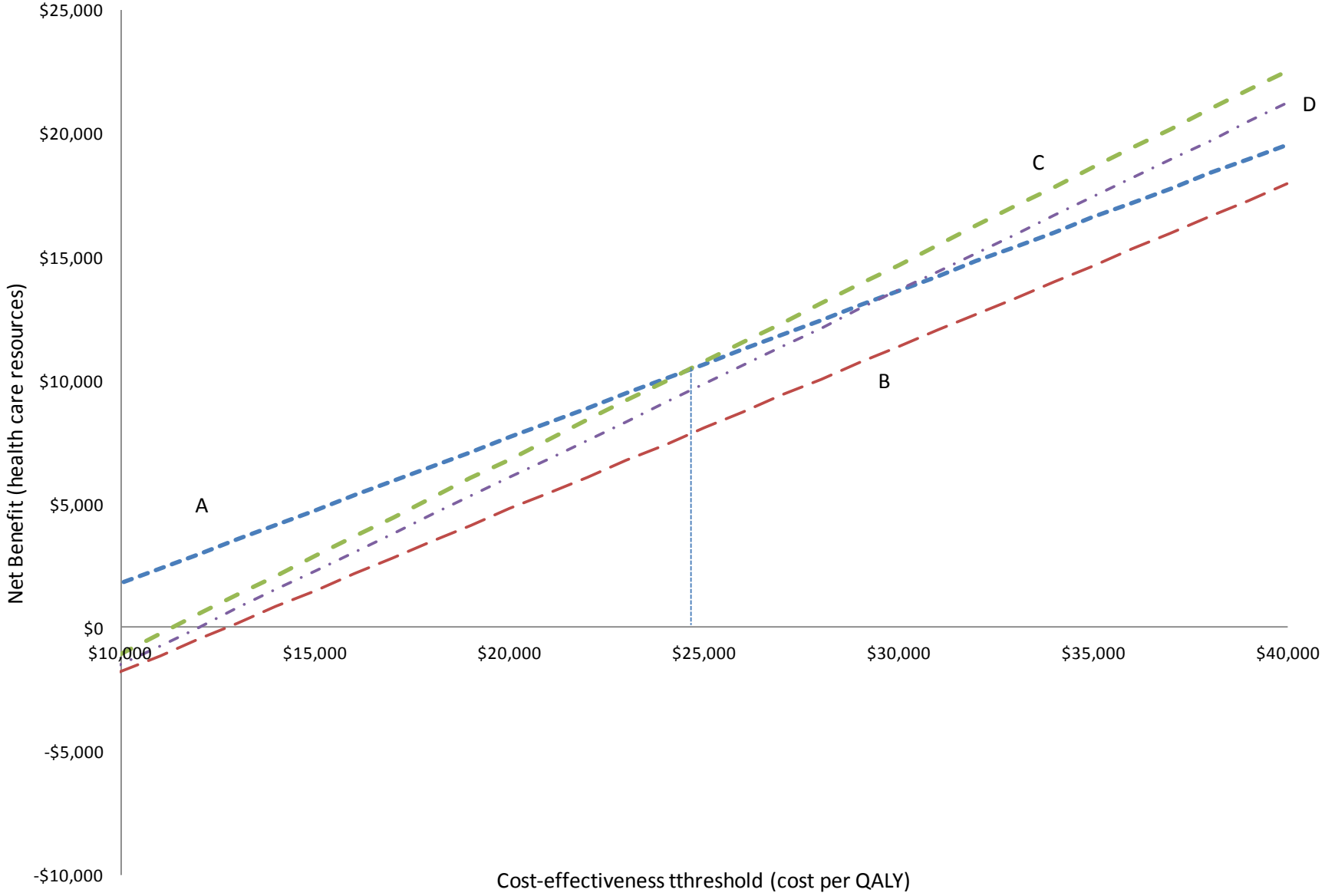
			ICERs compared to			Net benefit	
	Cost	QALYs	Lowest cost (A)	Next lowest cost	Relevant alternative	$20,000 per QALY	$30,000 per QALY
A	$4,147	0.593	-	-	-	**$7,713**	$13,643
B	$8,363	0.658	$64,862	$64,862	ED	$4,797	$11,377
C	$8,907	0.787	$24,536	$4,217	$24,536	$6,833	**$14,703**
D	$9,078	0.758	$29,885	SD	SD	$6,082	$13,662

SD = strongly dominated
ED = extendedly dominated

Comparing multiple alternatives



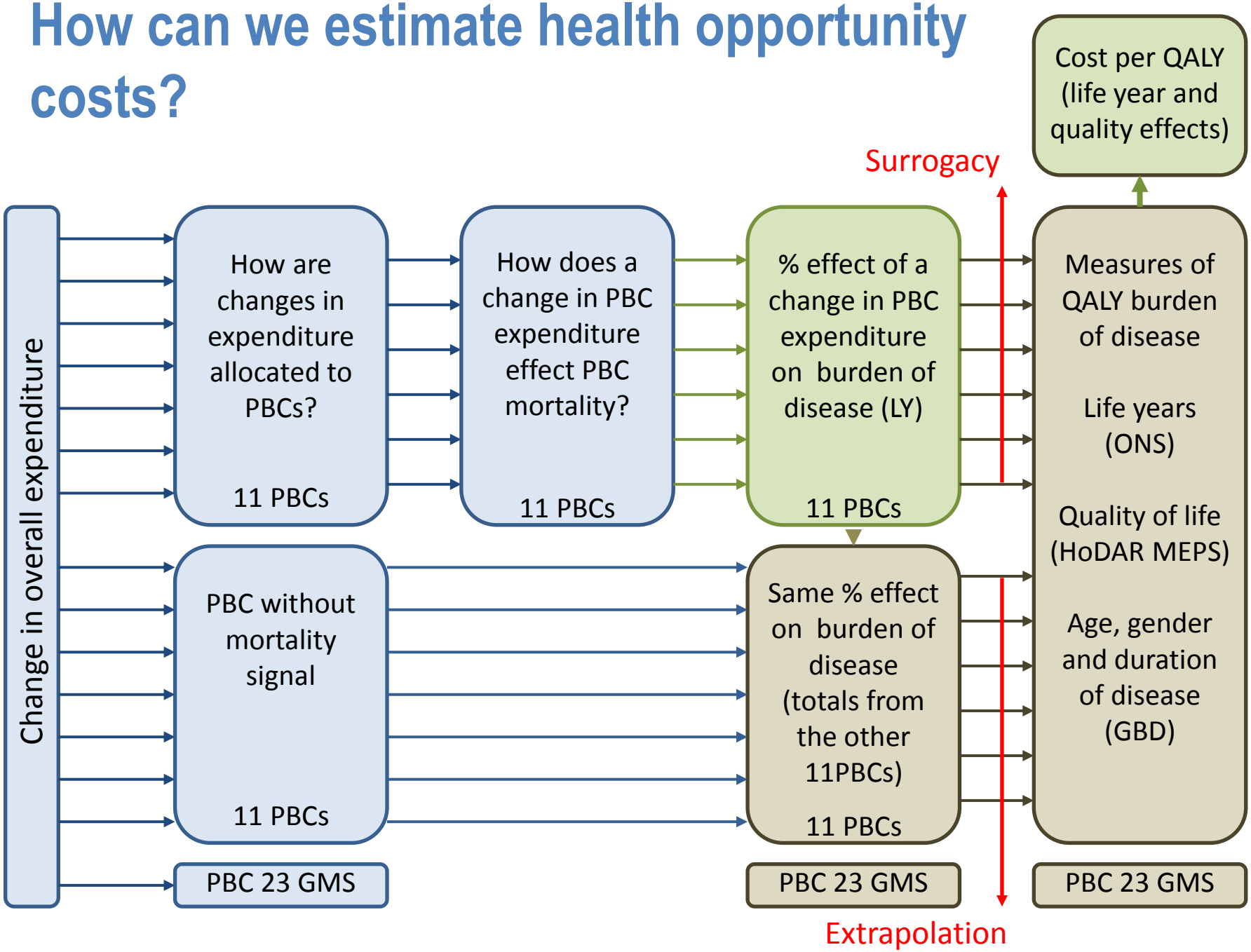
Comparing multiple alternatives



Which cost-effectiveness threshold?

- Norms describing how recommendations are made
  - NICE (2004), £20,000 to £30,000 per QALY
  - Does not reject below £30,000 per QALY
  - Evidence that the effective threshold is £42,000 per QALY
  - In some circumstances £50,000 per QALY
- Health opportunity costs (supply side)
  - What we must give up to accommodate a proposed investment
  - What else could have done with the additional resources required
  - Health effects of changes in health expenditure
- What its not
  - Consumption value of health (willingness to pay, v)
  - Marginal productivity of ‘ideal’ health care system

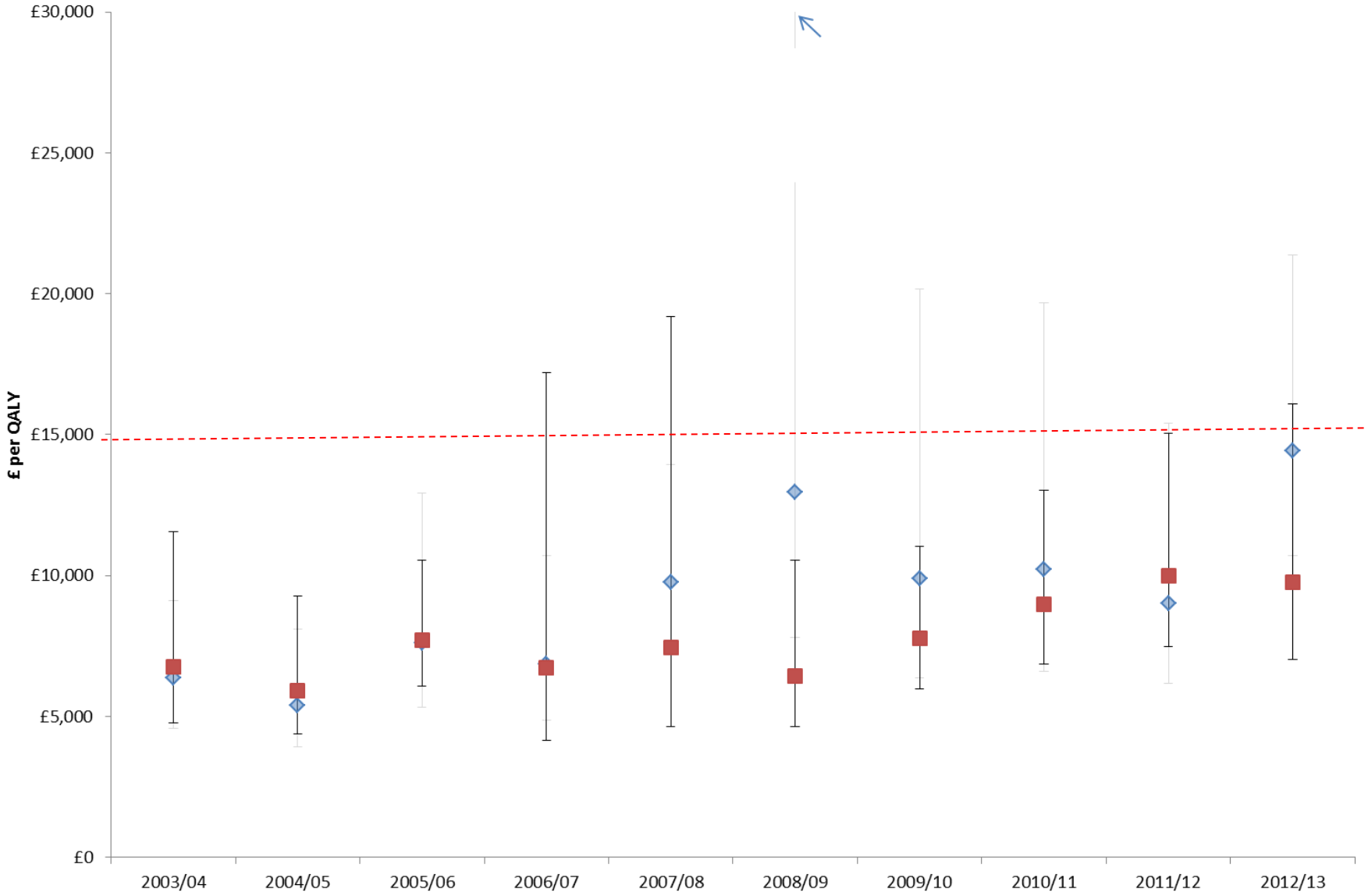
How can we estimate health opportunity costs?



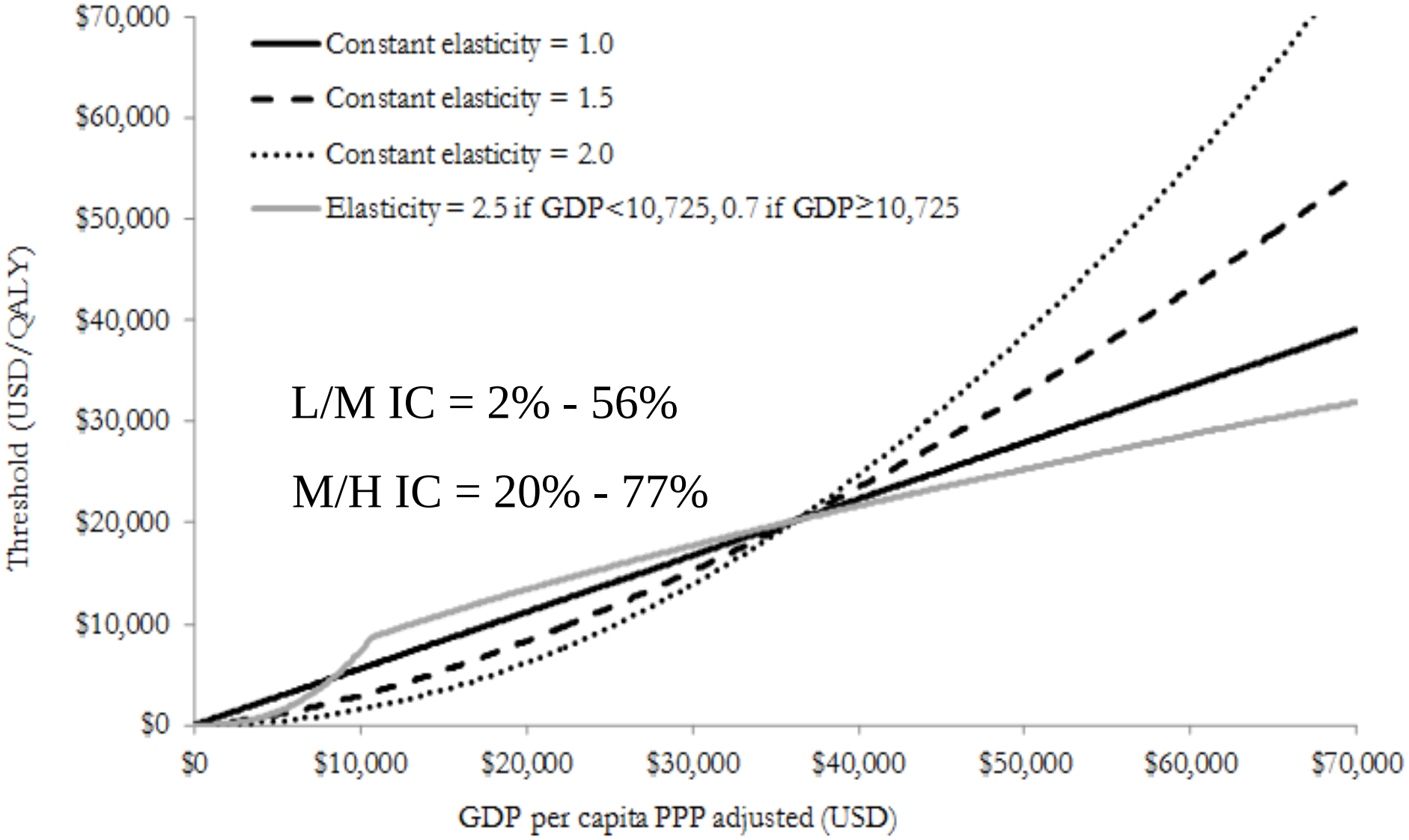
What are the expected health consequences of £10m?

	Change in spend	Additional deaths	LY lost	Total QALY lost	Due to premature death	Quality of life effects
Totals	**10 (£m)**	**51**	**233**	**773**	**150**	**623**
Cancer	0.45	3.74	**37.5**	26.3	24.4	1.9
Circulatory	0.76	22.78	**116.0**	107.8	73.7	34.1
Respiratory	0.46	13.37	**16.1**	229.4	10.1	**219.3**
Gastro-intestinal	0.32	2.62	**24.7**	43.9	16.2	27.7
Infectious diseases	0.33	0.72	5.3	15.7	3.6	12.1
Endocrine	0.19	0.67	5.0	60.6	3.2	57.3
Neurological	0.60	1.21	6.5	109.1	4.3	**104.8**
Genito-urinary	0.46	2.25	3.3	10.6	2.1	8.5
Trauma & injuries*	0.77	0.00	0.0	0.0	0.0	0.0
Maternity & neonates*	0.68	0.01	0.4	0.2	0.2	0.1
Disorders of Blood	0.21	0.36	1.7	21.8	1.1	20.7
Mental Health	1.79	2.83	12.8	95.3	8.3	**87.0**
Learning Disability	0.10	0.04	0.2	0.7	0.1	0.6
Problems of Vision	0.19	0.05	0.2	4.2	0.2	4.1
Problems of Hearing	0.09	0.03	0.1	14.0	0.1	13.9
Dental problems	0.29	0.00	0.0	6.8	0.0	6.8
Skin	0.20	0.24	1.1	1.9	0.7	1.2
Musculo skeletal	0.36	0.39	1.8	23.2	1.2	22.1
Poisoning and AE	0.09	0.04	0.2	0.8	0.1	0.7
Healthy Individuals	0.35	0.03	0.2	0.7	0.1	0.6
Social Care Needs	0.30	0.00	0.0	0.0	0.0	0.0
Other (GMS)	1.01	0.00	0.0	0.0	0.0	0.0

Re-estimated for all waves of data



Possible implications for other countries

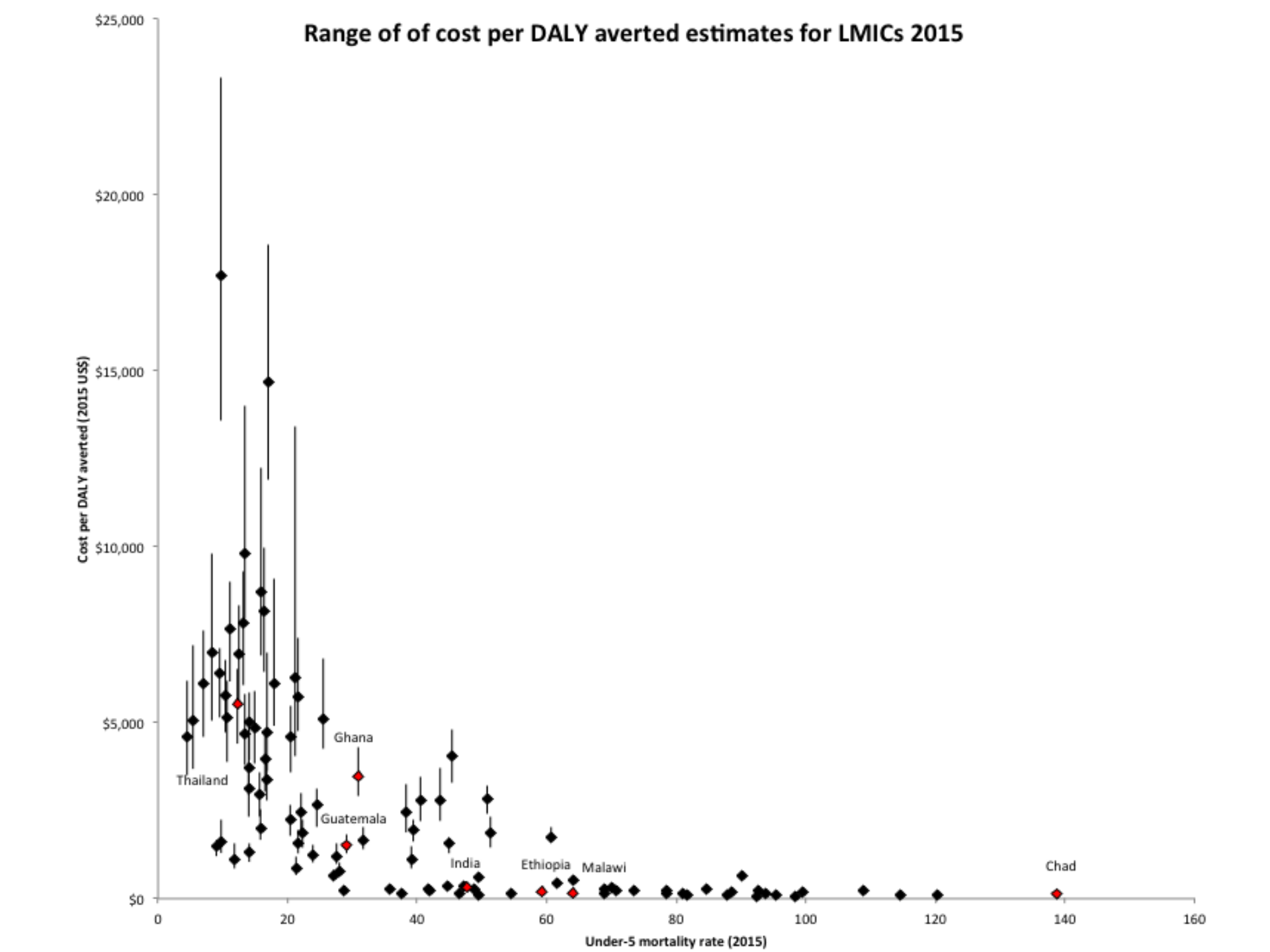


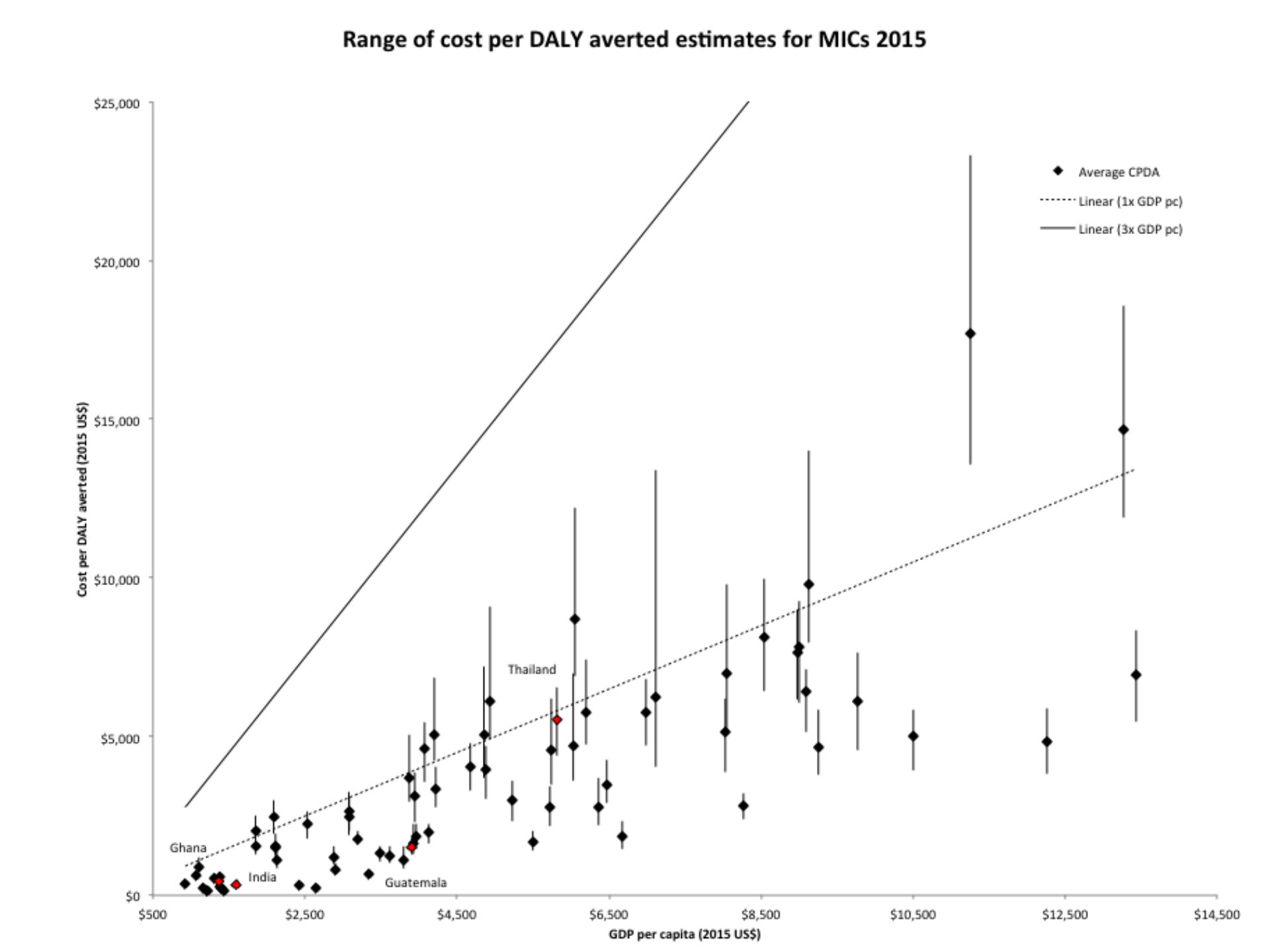
Other estimates using within country data

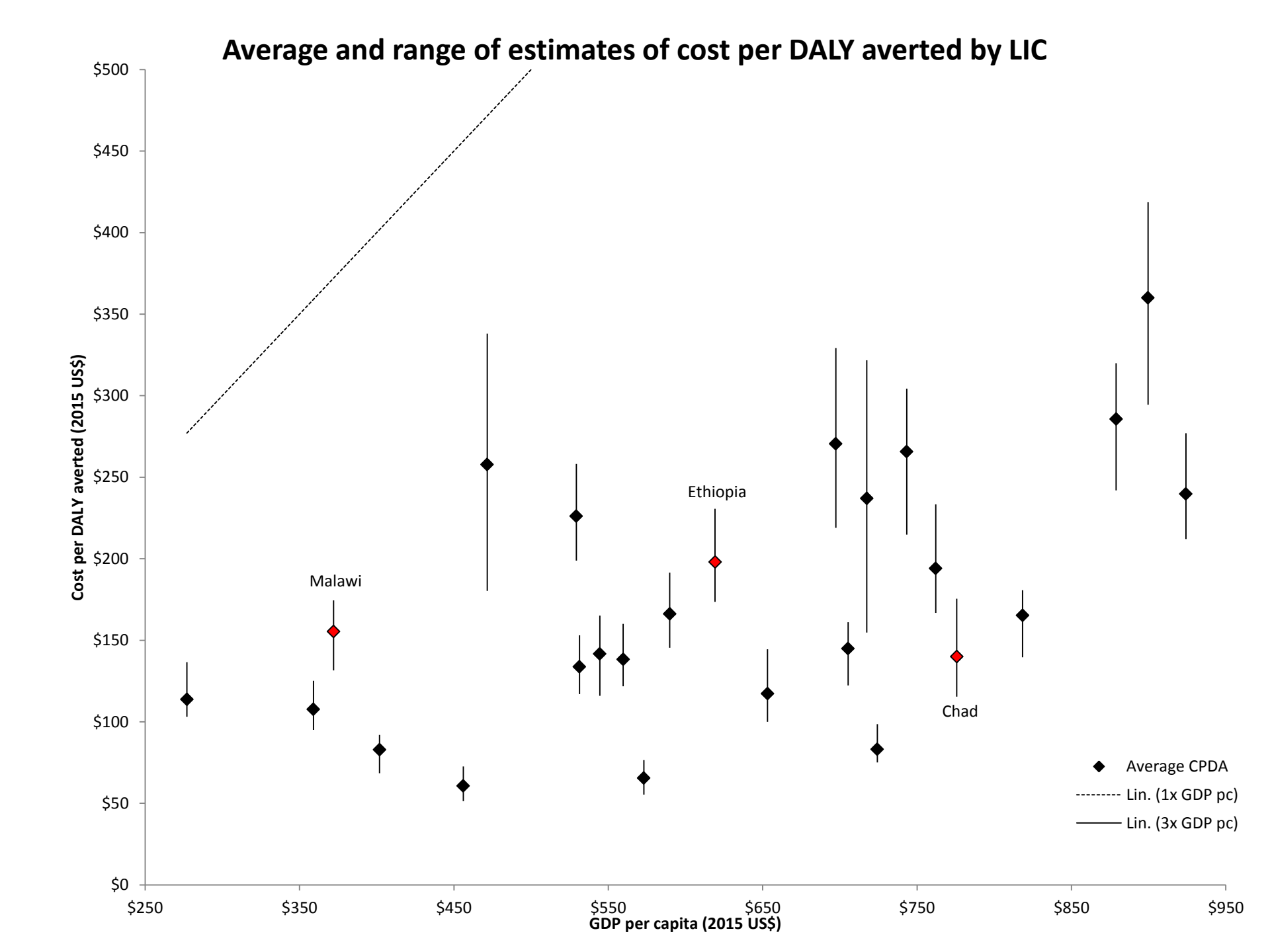
- Australia (Edney et al)
  - $28,033 per QALY AUD ($20,758 to $37,667)
- Spain (Vallejo-Torres et al)
  - 22,000€ to 25,000€ per QALY
- Netherlands (van Baal)
  - 41,000€ per QALY (CVD hospital care only)
- Sweden (Siverskog and Henriksson)
  - 39,000€ per QALY
- Indonesia (Kreif et al)
  - $331 per DALY averted (USD)
- South Africa (Edoka and Hofman)
  - $3,000 per DALY averted (USD)

Estimates of the effect of expenditure on mortality

- Bokhari et al 2007
  - Estimated elasticities for 127 countries
  - Effect of expenditure on under 5 and maternal mortality
  - Account for endogeneity in health expenditure and GDPpc
  - Interaction with measures of infrastructure and donor funding
- Ochalek et al 2018
  - Re-estimate effect on adult mortality (male and female)
  - Population (age and gender), mortality rates (age and gender), conditional life expectancies (age and gender), total health care expenditure
  - Country specific cost per life year and costs per DALY
  - Directly re-estimated for direct effects on YLL, YLD and DALY


Range of of cost per DALY averted estimates for LMICs 2015
$25,000
$20,000
$15,000
$10,000
$5,000
$0
Cost per DALY averted (2015 US$)
0
20
40
60
80
100
120
140
160
Under-5 mortality rate (2015)
Thailand
Ghana
Guatemala
India
Ethiopia
Malawi
Chad


Range of cost per DALY averted estimates for MICs 2015
$25,000
$20,000
$15,000
$10,000
$5,000
$0
Cost per DALY averted (2015 US$)
$500
$2,500
$4,500
$6,500
$8,500
$10,500
$12,500
$14,500
GDP per capita (2015 US$)
Average CPDA
Linear (1x GDP pc)
Linear (3x GDP pc)
Thailand
Ghana
India
Guatemala


Average and range of estimates of cost per DALY averted by LIC
$500
$450
$400
$350
$300
$250
$200
$150
$100
$50
$0
Cost per DALY averted (2015 US$)
$250
$350
$450
$550
$650
$750
$850
$950
GDP per capita (2015 US$)
Malawi
Ethiopia
Chad
Average CPDA
Lin. (1x GDP pc)
Lin. (3x GDP pc)

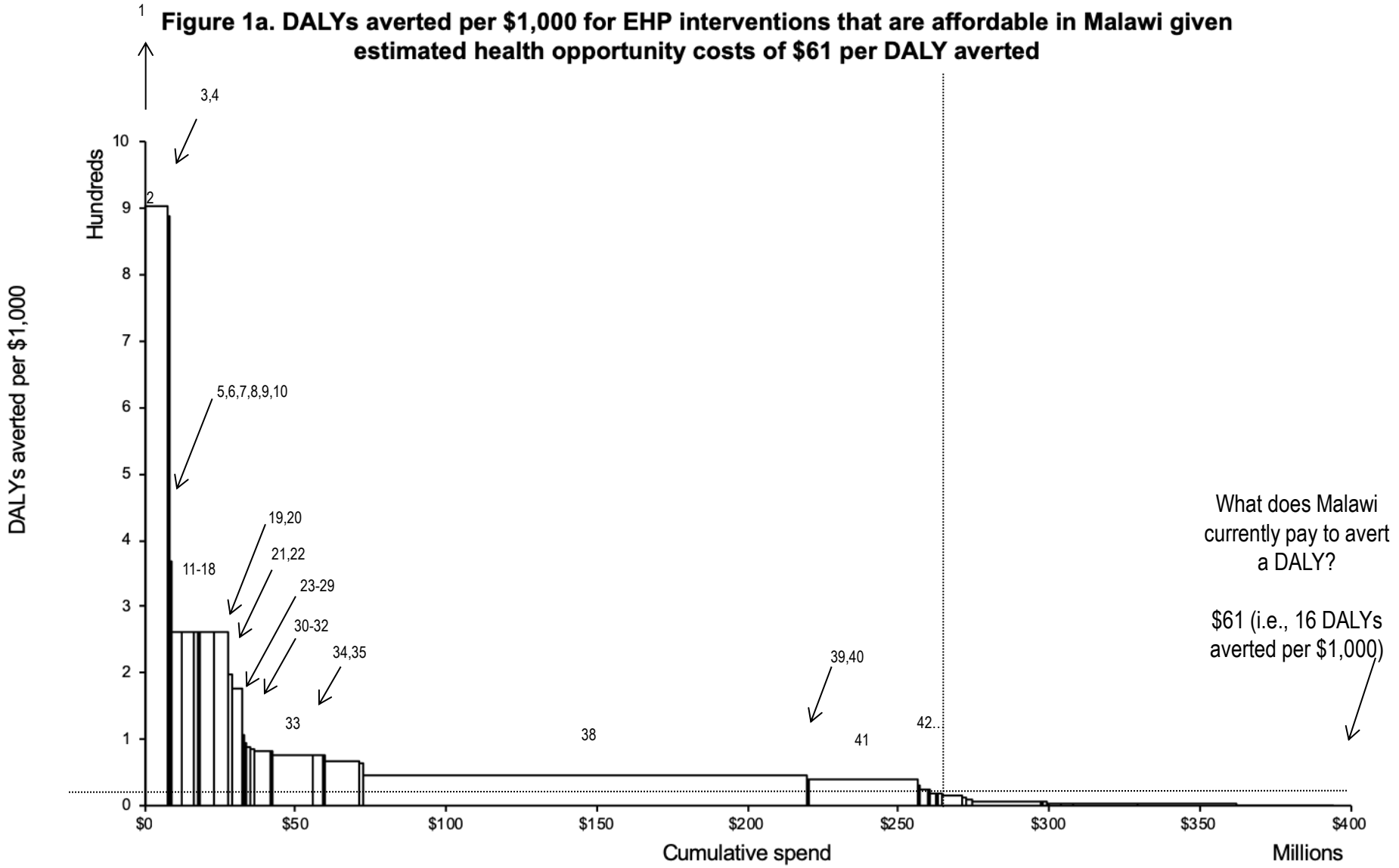
Non-mutually-exclusive alternatives

- Comparing non-mutually-exclusive alternatives
  - Same disease and intervention but for different population subgroups
    - Different decisions for different subgroups
    - Approve for some, non or all
  - Diverse heath care programmes
    - What should be removed/added to benefits package
    - How should we construct a new benefits package
- Three alternatives
  - Use an estimate of health opportunity costs (threshold)
  - League table of ICERs (implies a threshold)
  - Mathematical programming solutions (solves for threshold)

League tables of cost-effectiveness ratios

- Rank all programmes by ICER
- Implement until exhaust the budget
- Threshold = ICER of last (marginal) project determined by the budget
- Problems
  - Not just one ICER per programme
  - Include all in ‘cells’ and account of dominated extendedly dominated?
  - Full information

Figure 1a. DALYs averted per $1,000 for EHP interventions that are affordable in Malawi given estimated health opportunity costs of $61 per DALY averted



Budget = $264.5 million

CHE
Centre For Health Economics

But making a lot of assumptions

- Perfect divisibility?
  - Indivisible relative to the budget (Birch 2006, Epstein et al 2007)
  - Horizontal equity as indivisibility (Stinnett and Paltiel, Epstein et al 2007)
- Uncertainty, variability and budgetary policies (McKenna et al 2010)
  - Decision rules are a very special case (soft constraint)
- Single constraint?
  - Multiple budgets
  - Budgets over time
  - Equity constraints

  } (Epstein et al 2007)
- Single sector?
  - Multi sector impacts (Claxton et al 2010)
- Implications
  - Complete and correct league tables cannot provide the 'optimal' solution
  - Mathematical programming solutions
    - But informational requirements are not feasible
  - Current 'rules' are partial and approximations

Mathematical programming

- Single health sector single constraint
  - maximise health outcome (H)
  - choose proportion (x) of population i that receives treatment j within programme *k*
  - Single budget constraint for health (C_H)
- Solve for 1/*k*

- Other constraints
  - Indivisibility, $X_{ijk} = 0,1$
  - Other equity issues, $X_{1jk} = X_{2jk}$
- CEA decision 'rules' don't work even if threshold = *k*

$$\max_{\Psi}\left(\sum_{k=1}^{K}\sum_{j=1}^{J_k}\sum_{i=1}^{I_k} H_{ijk}\, x_{ijk}\right)$$

$$\Psi = \left(x_{ijk}, i = 1\ldots I_k, j = 1\ldots J_k, k = 1\ldots K\right)$$

sto

$$\sum_{k=1}^{K}\sum_{j=1}^{J_k}\sum_{i=1}^{I_k} c_{ijk}^{H}\, x_{ijk} \le C_H$$

$$0 \le x_{ijk} \le 1 \qquad i = 1\ldots I_k, j = 1\ldots J_k, k = 1\ldots K$$

$$\sum_{j=1}^{J_k} x_{ijk} = 1 \qquad i = 1\ldots I_k, k = 1\ldots K$$

Which perspective?

- Costs and benefits fall on different sectors
  - Public sectors with constrained resources
  - Private sector
- No consensus what counts, how measure or value
  - Health, consumption and other social arguments
  - No complete, legitimate and explicit SWF
  - Other important arguments that are difficult to specify and measure
- Even if willing to impose a SWF
  - Implications of constraints on heath (and other public) expenditure
  - What other aspects of benefit are displaced?

Net production (marketed and non marketed) for a sample of ICD codes

Health care costs displace/gain health *and* other aspects of value too

NHS£12,936 to displace/gain a QALY

£11,611 of net production for every QALY displaced/gained

1.1 NHS£ per net production £
(1.1 = £12,936/£11,811)

Wider Social Benefits (net production)		
M05	Rheumatoid arthritis	£30,034
E11	Diabetes	£27,421
M45	Ankylosing spondylitis	£26,190
F30	Depression	£23,489
F20	Schizophrenia	£22,697
J45	Asthma	£20,100
M81	Osteoporosis	£17,910
G35	Multiple sclerosis	£15,482
J43	Emphysema and COPD	£14,525
G40	Epilepsy	£14,245
L40	Psoriasis	£11,890
Displaced	**Average of displaced QALYs**	**£11,611**
E66	Obesity	£8,138
C53	Cervical cancer	£6,912
K50	Irritable Bowel Syndrome	£6,284
J30	Allergic rhinitis	£5,234
G20	Parkinson's disease	£3,102
C50	Breast cancer	£2,888
G30	Alzheimer's disease	£351
A40	Streptococcal septicaemia	-£513
F03	Dementia	-£2,430
I64	Stroke	-£6,949
C18	Colon cancer	-£8,061
C61	Prostate cancer	-£10,602
C64	Kidney cancer	-£13,211
I21	Acute myocardial infarction	-£14,395
I26	Embolisms, fibrillation, thrombosis	-£16,752
J10	Influenza	-£21,568
C90	Myeloma	-£23,382
C92	Myeloid leukaemia	-£24,813
C22	Liver cancer	-£32,709
C34	Lung cancer	-£36,067
C25	Pancreatic cancer	-£53,860

Other aspects of value

- Appraisal of ranibizumab (Lucentis) for diabetic macular oedema 2011
  - Retinal thickness ≥ 400 subgroup before PAS
  - Additional costs = £3,506 per patient
  - Incremental cost-effectiveness = £25,000 per QALY
  - 23,000 eligible patients each year

Attributes	Investment	Disinvestment	Net effects
	Lucentis for diabetic macular oedema (£80m pa)	Expected effects of £80m pa	
Deaths	0	-411	-411
Life years	0	- 1,864	-1,864
QALYs	3,225	- 6,184	-2,959
Severity of disease QALY loss	2.68	2.07	0.61
Wider social benefits Consumption	£88.4m	- £71.8m	£16.6m

How should we decide?

- Restrict to health and health care
  - Net health benefits = 3,225 – 6,184 = - 2,959 QALYs

$$\Delta h - \frac{\Delta c_h}{k} > 0$$

- A single societal perspective
  - Ignore the constraint ?
    - Net costs = £80m - £88.4m = - £8.4m

$$\Delta h - \frac{\Delta c_h + \Delta c_c}{k} > 0$$

How should we decide?

- A single societal perspective
  - Account for the constraint
    - Net health loss = -2,959 QALYs
    - Wider social benefits = £88.4m
    - Worthwhile if consumption value of health < £29,875 per QALY

$$\left[\Delta h - \frac{\Delta c_h}{k}\right] - \frac{\Delta c_c}{v} > 0$$

  - Account for displaced wider social benefits
    - Net health loss = -2,959 QALYs
    - Net wider social benefits = £88.4m – £71.8m = £16.6m
    - Worthwhile if consumption value of health < £5,610 per QALY

$$\left[\Delta h - \frac{\Delta c_h}{k_h}\right] - \left[\frac{\Delta c_c + k_c.\Delta c_h}{v}\right] > 0$$

$$k_c = £11{,}811 / £12{,}936 = 0.91 \left(Net\ production £\ per NHS £ \right)$$

Accounting for the timing of costs and health benefits

- Project costs £1m now and generates 100 QALYs in year 10

0	1	2	3	10
£1m				100 QALYs

Accounting for the timing of costs and health benefits

- Project costs £1m now and generates 100 QALYs in year 10

0	1	2	3	10
£1m				100 QALYs
		Cost per QALY = £14,106		£1,410,599 100 QALYs

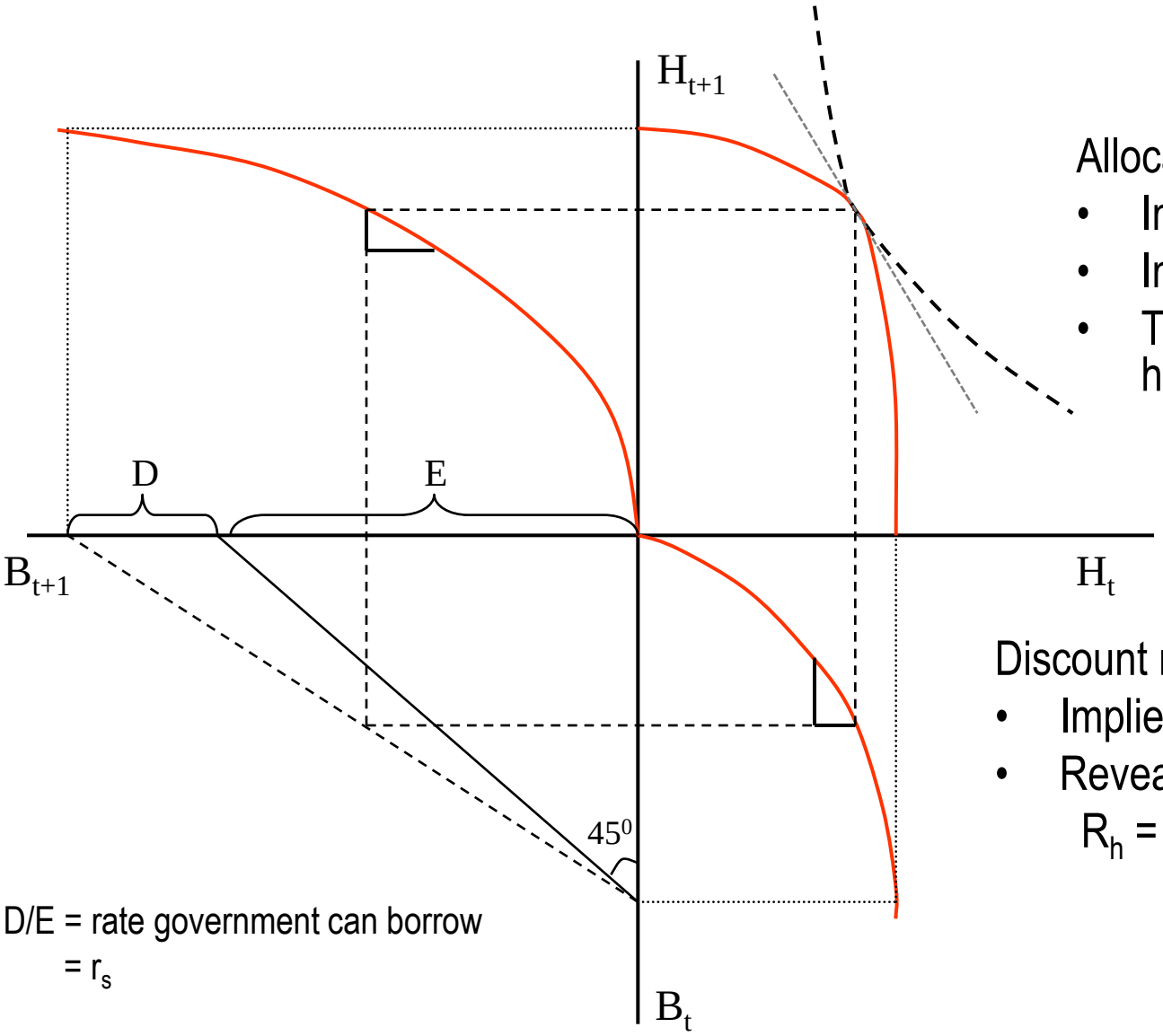
Accounting for the timing of costs and health benefits

- Project costs £1m now and generates 100 QALYs in year 10

0	1	2	3	10
£1m				100 QALYs
			Cost per QALY = £14,106	£1,410,599 100 QALYs
£1m 70.9 QALYs	Cost per QALY = £14,106			

- Health is tradable over time
  - Even for an individual (Grossman) although limits
- Health care turns resources into health
  - If its sensible to discount health care costs it must be sensible to discount health (they are the same thing)
- But what rate?
- Should it be the same rate for costs and benefits?

What discount rate for health (r_h)?



D/E = rate government can borrow
= r_s

Allocating budget over time

- Implies k_t and k_{t+1}
- Implies H_t and H_{t+1}
- Trade current and future health (R_h)

Discount rate for health

- Implied by budget allocation
- Revealed social preference

$R_h = r_s - g_k$

Project with health benefits and health care costs

	Effects of the project		Health Effects		Equivalent heath care resources		Equivalent consumption effects	
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Time	**Additional health benefits**	**Additional health care costs**	**Benefits**	**Costs**	**Benefits**	**Costs**	**Benefits**	**Costs**
1	Δh_1	Δc_{h1}	Δh_1	$\Delta c_{h1}/k_{h1}$	$k_{h1}.\Delta h_1$	Δc_{h1}	$V_{h1}.\Delta h_1$	$V_{h1}(\Delta c_{h1}/k_{h1})$
..	..	..	..	..	..	..	..	..
t	Δh_t	Δc_{ht}	Δh_t	$\Delta c_{ht}/k_{ht}$	$k_{ht}.\Delta h_t$	Δc_{t1}	$V_{ht}.\Delta h_t$	$V_{ht}(\Delta c_{ht}/k_{ht})$
..	..	..	..	..	..	..	..	..
T	Δh_T	Δc_{hT}	Δh_T	$\Delta c_{hT}/k_{hT}$	$k_{hT}.\Delta h_T$	Δc_{hT}	$V_{hT}.\Delta h_T$	$V_{hT}(\Delta c_{hT}/k_{hT})$

How should these streams be discounted?	$D_h = r_s - gk_h$	$D_h = r_s$	$r_c = \delta + \eta g_c$

Using incremental cost-effectiveness ratios?

- Any expected growth in k_h means future costs are less important (health opportunity costs are lower)
  - Discount cost at a lower rate than health
  - Dh = r_h
  - Dc = $r_h + g_k$

- Any expected growth in v_h means future health benefits and opportunity costs are more important (health opportunity costs are lower)
  - Discount health benefits and health care costs at a lower rate
  - Dh = $r_c - g_v$
  - Dc = $r_c - g_v + g_k$

Effects on health, health care costs and consumption

	Effects of the project			Effects on heath	Effects on consumption
(1)	(2)	(3)	(4)	(5)	(6)
Time	**Additional health benefits**	**Additional health care costs**	**Consumption costs**	**Net health benefits**	**Net consumption costs**
1	Δh_1	Δc_{h1}	Δc_{c1}	$\Delta h_1 - \Delta c_{h1} / k_{h1}$	$\Delta c_{c1} + k_{c1}. \Delta c_{h1}$
..	..	..	..	..	..
t	Δh_t	Δc_{ht}	Δc_{ct}	$\Delta h_t - \Delta c_{ht} / k_{ht}$	$\Delta c_{ct} + k_{ct}. \Delta c_{ht}$
..	..	..	..	..	..
T	Δh_T	Δc_{hT}	Δc_{cT}	$\Delta h_T - \Delta c_{hT} / k_{hT}$	$\Delta c_{cT} + k_{cT}. \Delta c_{hT}$

Effects on health, health care costs and consumption

	Net effects		
(1)	(2)	(3)	(4)
Time	**Equivalent consumption effects**	**Equivalent health effects**	**Equivalent health care resources**
1	$v_{h1}(\Delta h_1-\Delta c_{h1}/k_{h1}) - (\Delta c_{c1}+k_{c1}.\Delta c_{h1})$	$(\Delta h_1-\Delta c_{h1}/k_{h1}) - (\Delta c_{c1}+k_{c1}.\Delta c_{h1})/v_{h1}$	$k_{h1}((\Delta h_1-\Delta c_{h1}/k_{h1}) - (\Delta c_{c1}+k_{c1}.\Delta c_{h1})/v_{h1})$
..	..	..	..
t	$v_{ht}(\Delta h_t-\Delta c_{ht}/k_{ht}) - (\Delta c_{ct}-k_{ct}.\Delta c_{ht})$	$(\Delta h_t-\Delta c_{ht}/k_{ht}) - (\Delta c_{ct}+k_{ct}.\Delta c_{ht})/v_{ht}$	$k_{ht}((\Delta h_t-\Delta c_{ht}/k_{ht}) - (\Delta c_{ct}+k_{ct}.\Delta c_{ht})/v_{ht})$
..	..	..	..
T	$v_{hT}(\Delta h_T-\Delta c_{hT}/k_{hT}) - (\Delta c_{cT}-k_{cT}.\Delta c_{hT})$	$(\Delta h_T-\Delta c_{hT}/k_{hT}) - (\Delta c_{cT}+k_{cT}.\Delta c_{hT})/v_{hT}$	$k_{hT}((\Delta h_T-\Delta c_{hT}/k_{hT}) - (\Delta c_{cT}+k_{cT}.\Delta c_{hT})/v_{hT})$

Aggregating effects across countries or jurisdictions

	Equivalent consumption effects across countries or jurisdictions		
	Country *A*	**Country *B***	**Country *C***
Effects in period t	$v_{h,t}^{A}\left[\Delta h_t^{A}-\frac{\Delta c_{h,t}^{A}}{k_{h,t}^{A}}\right]-\left[\Delta c_{c,t}^{A}+k_{c,t}^{A}.\Delta c_{h,t}^{A}\right]$	$v_{h,t}^{B}\left[\Delta h_t^{B}-\frac{\Delta c_{h,t}^{B}}{k_{h,t}^{B}}\right]-\left[\Delta c_{c,t}^{B}+k_{c,t}^{B}.\Delta c_{h,t}^{B}\right]$	$v_{h,t}^{C}\left[\Delta h_t^{C}-\frac{\Delta c_{h,t}^{C}}{k_{h,t}^{C}}\right]-\left[\Delta c_{c,t}^{C}+k_{c,t}^{C}.\Delta c_{h,t}^{C}\right]$
Net present value	$\sum_{t=1}^{T}\frac{v_{h,t}^{A}\left[\Delta h_t^{A}-\frac{\Delta c_{h,t}^{A}}{k_{h,t}^{A}}\right]-\left[\Delta c_{c,t}^{A}+k_{c,t}^{A}.\Delta c_{h,t}^{A}\right]}{\left(1+r_c^{A}\right)^{t}}$	$\sum_{t=1}^{T}\frac{v_{h,t}^{B}\left[\Delta h_t^{B}-\frac{\Delta c_{h,t}^{B}}{k_{h,t}^{B}}\right]-\left[\Delta c_{c,t}^{B}+k_{c,t}^{B}.\Delta c_{h,t}^{B}\right]}{\left(1+r_c^{B}\right)^{t}}$	$\sum_{t=1}^{T}\frac{v_{h,t}^{C}\left[\Delta h_t^{C}-\frac{\Delta c_{h,t}^{C}}{k_{h,t}^{C}}\right]-\left[\Delta c_{c,t}^{C}+k_{c,t}^{C}.\Delta c_{h,t}^{C}\right]}{\left(1+r_c^{C}\right)^{t}}$
Global net present value	$\sum_{t=1}^{T}\frac{v_{h,t}^{A}\left[\Delta h_t^{A}-\frac{\Delta c_{h,t}^{A}}{k_{h,t}^{A}}\right]-\left[\Delta c_{c,t}^{A}+k_{c,t}^{A}.\Delta c_{h,t}^{A}\right]}{\left(1+r_c^{A}\right)^{t}}+\sum_{t=1}^{T}\frac{v_{h,t}^{B}\left[\Delta h_t^{B}-\frac{\Delta c_{h,t}^{B}}{k_{h,t}^{B}}\right]-\left[\Delta c_{c,t}^{B}+k_{c,t}^{B}.\Delta c_{h,t}^{B}\right]}{\left(1+r_c^{B}\right)^{t}}+\sum_{t=1}^{T}\frac{v_{h,t}^{C}\left[\Delta h_t^{C}-\frac{\Delta c_{h,t}^{C}}{k_{h,t}^{C}}\right]-\left[\Delta c_{c,t}^{C}+k_{c,t}^{C}.\Delta c_{h,t}^{C}\right]}{\left(1+r_c^{C}\right)^{t}}$		

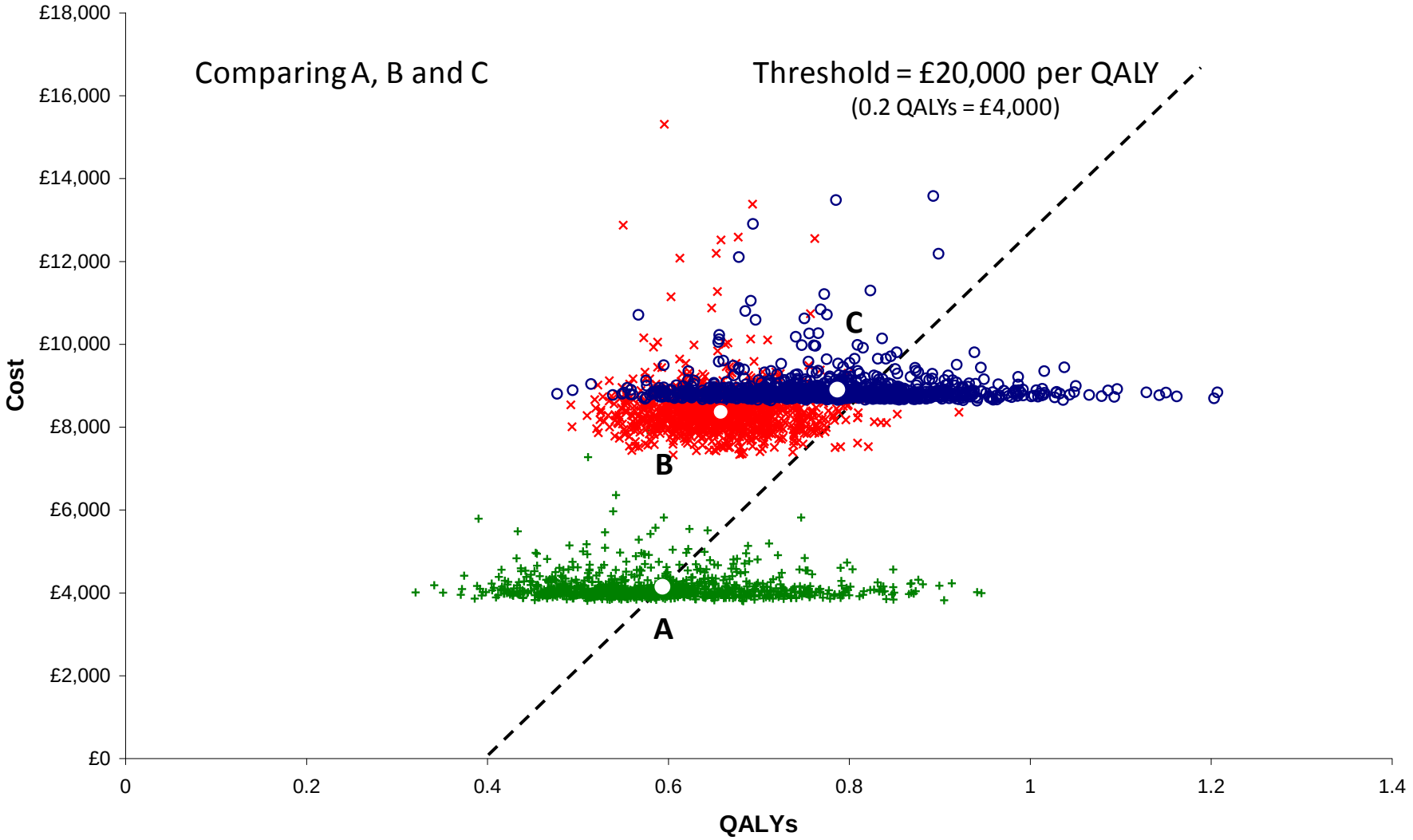
Key quantity		Possible default estimates
Health opportunity costs of health care expenditure	k_{ht}	• Estimates for most LMICs for 2015 expenditure provide useful initial defaults • Initial projections of these estimates based on other published projections of health expenditure and consumption are also available • These initial country specific estimates can be refined and updated as other country specific estimates emerge, ideally using within country data where this is possible.
Consumption opportunity costs of health care expenditure	k_{ct}	• Default assumption of 1 (1$ spent on health care delivers 1$ in net production or consumption opportunities) • Default assumption that the real value of the net production effects of the health effects of changes in health expenditure will grow at g_c
Consumption value of health and its evolution over time	v_{ht}	• Estimating v_h (see other methods papers) • Evolution of v_{ht} based on growth in consumption (which is already required for r_c) and a default assumption about the income elasticity of demand for health. • A default assumption of an income elasticity of demand for health of 1 (v_{ht} would grow at gc) • Alternative scenarios based on evidence that income elasticity is likely to differ.
Other sectors	v_{xt}/k_{xt}	• Default assumption that $v_{ht}/k_{ht} = v_{xt}/k_{xt}$ when considering impacts on public sectors
Time preference for consumption	r_c	• Default normative assumption $\delta = 0$ for social choices • Default assumption that $\eta = 1$, so $r_c = g_c$ (reported as expected growth in measures of national income per capita for that country). • Alternative scenarios based on evidence or reasoning of why η is likely to differ in specific contexts or different judgements about g_c • As evidence for values of η specific to LMICs evolves and estimates of economics growth are revised these defaults can be updated.

Key quantity	Possible default estimates
Catastrophic risk	• Exclude catastrophic risk from a common discount rate for consumption effects ($\delta=0$) • Elicited probabilities of truly catastrophic events ($\delta<0.1\%$)
Project specific risks	• Project specific risks should be included in the analysis and how 'consumption equivalent' time streams of effects are estimated rather than in a project specific discount rate.
Macroeconomic risk and prudential saving	• No adjustment for macroeconomic risk for projects with time horizons less than 40 years • Longer time horizons or where macroeconomic risk is greater and increases more rapidly with term declining rates should be based only on the nonlinear effects of uncertainty • Since growth and uncertainty about that growth will be country specific any decline in r_c will necessarily be country specific. • Any declining rates for r_c should be based on an initial assumption of beta=1 for all projects
Interaction of project specific and macroeconomic risk	• A qualitative indication of whether or not projects are likely to be strongly pro or counter cyclical should be provided • Further research is required on how the effects of these interactions might be best quantified for these types of project relevant to LMICs.

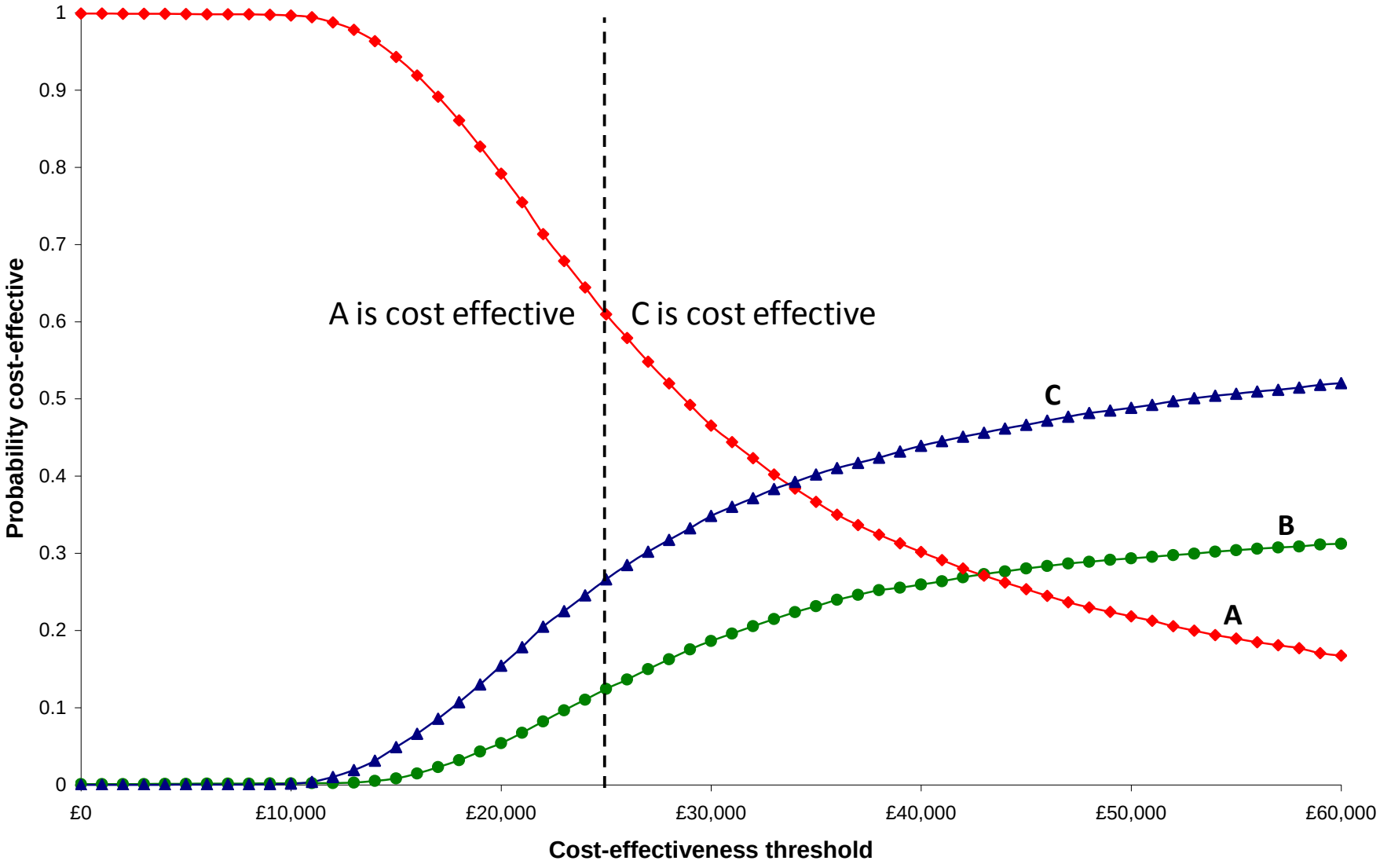
Some definitions

- What matters?
  - Health (gained and forgone)
  - Net health benefits (NHB)
- Uncertainty
  - Estimates of average NHB for a target population are imprecise
- Variability
  - Differences in NHB within a target population
  - Reasons for differences can not be observed
- Heterogeneity
  - Sources of variability that can be observed (payer or individual)
  - Can inform payer and individual decisions

Characterising uncertainty



Characterising uncertainty

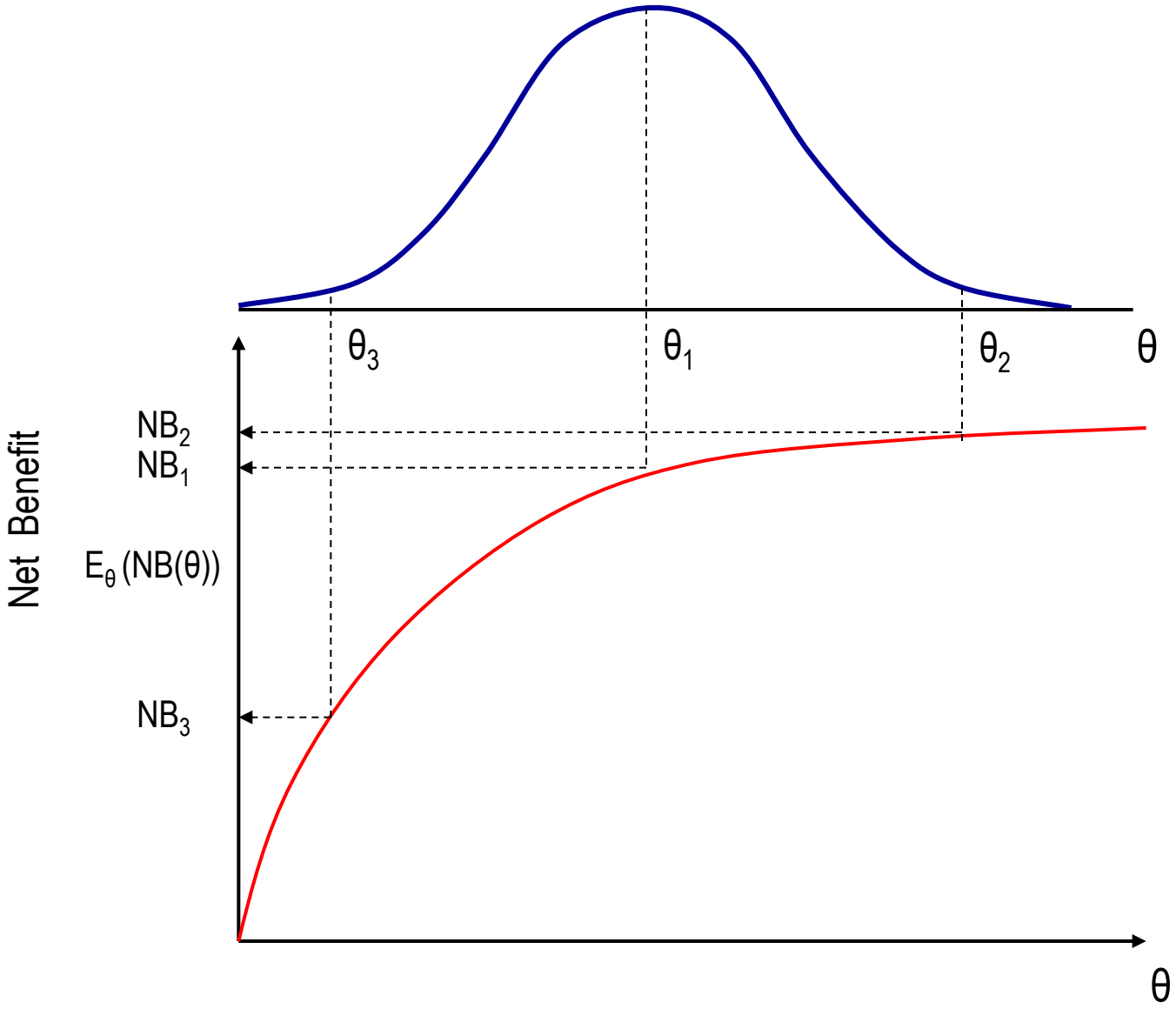


Characterising uncertainty

				Threshold = £20,000 per QALY			Threshold = £30,000 per QALY		
	Cost	QALYs	ICER	Net Benefit	Probability	P(error)	Net Benefit	Probability	P(error)
A	$4,147	0.593	-	$7,722	0.792	0.208	$13,656	0.465	
B	$8,363	0.658	ED	$4,794	0.054		$11,373	0.186	
C	$8,907	0.787	£24,628	$6,827	0.154		$14,695	0.348	0.652

But why does it matter?

Expected cost and effect



Would more evidence improve health?

How things could turn out	Net Health Benefit			Best we could do if we knew
	Treatment A	Treatment B	Best choice	
θ1	8	12	B	12
θ2	16	8	A	16
θ3	9	14	B	14
θ4	12	10	A	12
θ5	10	16	B	16
Average	**11**	**12**		**14**

What's the best we can do now?

Choose B

Expect 12 QALYs, gain 1 QALY

But uncertain

Wrong decision 2/5 times (error probability = 0.4)

Could we do better?

If we knew

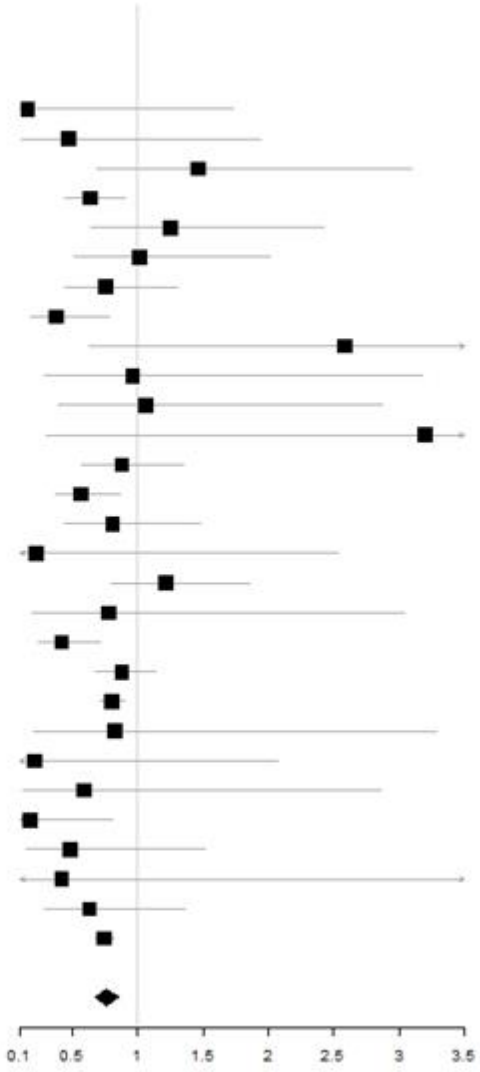
Expect 14 QALYs

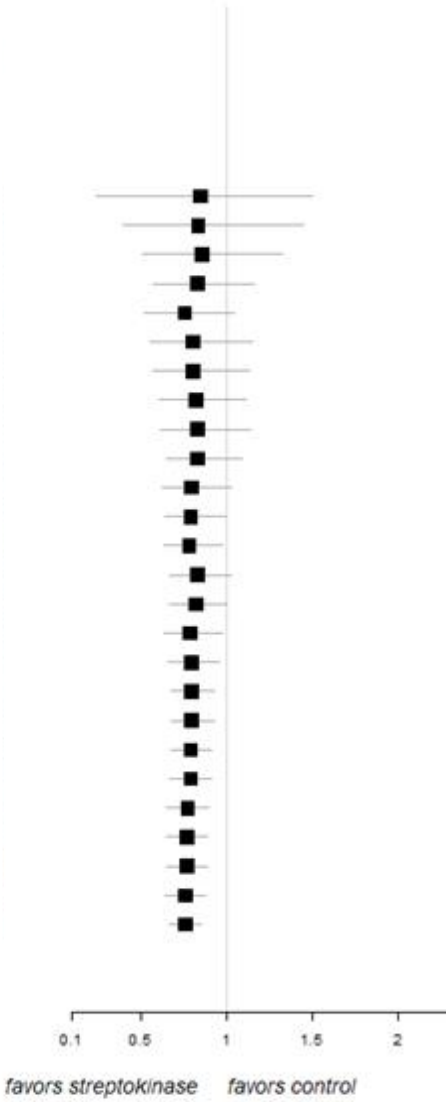
$$EVPI = E_\theta \max_j NB(j, \theta) - \max_j E_\theta NB(j, \theta) = 2 \text{ QALYs per patient}$$

Value of implementation and the value of information

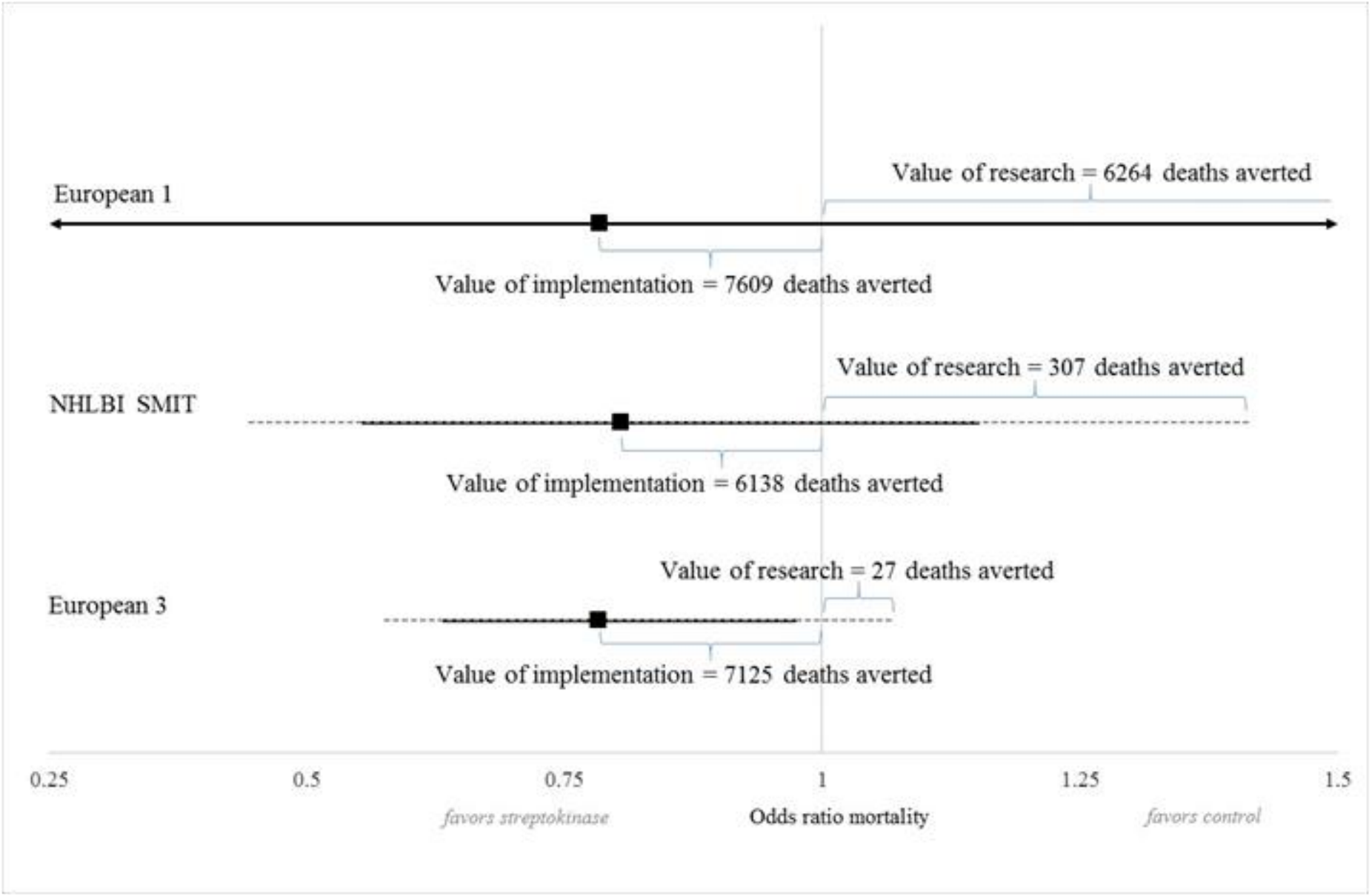
The sequence of trials of early thrombolysis using streptokinase

Study	Year	Streptokinase deaths/n	Control deaths/n	OR	95% CI
Fletcher	1959	1/12	4/11	0.16	(0.01 - 1.73)
Dewar	1963	4/21	7/21	0.47	(0.11 - 1.94)
European 1	1969	20/83	15/84	1.46	(0.69 - 3.10)
European 2	1971	69/373	94/357	0.64	(0.45 - 0.90)
Heikinheimo	1971	22/219	17/207	1.25	(0.64 - 2.42)
Italian	1971	19/164	18/157	1.01	(0.51 - 2.01)
Australian	1973	26/264	32/253	0.75	(0.44 - 1.31)
Frankfurt 2	1973	13/102	29/104	0.38	(0.18 - 0.78)
NHLBI SMIT	1974	7/53	3/54	2.59	(0.63 -10.60)
Frank	1975	6/55	6/53	0.96	(0.29 - 3.19)
Valere	1975	11/49	9/42	1.06	(0.39 - 2.88)
Klein	1976	4/14	1/9	3.20	(0.30 -34.59)
UK Collab	1976	48/302	52/293	0.88	(0.57 - 1.35)
Austrian	1977	37/352	65/376	0.56	(0.36 - 0.87)
Australian 2	1977	25/112	31/118	0.81	(0.44 - 1.48)
Lasierra	1977	1/13	3/11	0.22	(0.02 - 2.53)
N Ger Collab	1977	63/249	51/234	1.22	(0.80 - 1.85)
Witchiz	1977	5/32	5/26	0.78	(0.20 - 3.04)
European 3	1979	25/156	50/159	0.42	(0.24 - 0.72)
ISAM	1986	124/859	142/882	0.88	(0.68 - 1.14)
GISSI-1	1986	628/5860	758/5832	0.80	(0.72 - 0.90)
Olson	1986	5/28	5/24	0.83	(0.21 - 3.29)
Schreiber	1986	1/19	4/19	0.21	(0.02 - 2.07)
Durand	1987	3/35	4/29	0.59	(0.12 - 2.86)
White	1987	2/79	12/93	0.18	(0.04 - 0.81)
Bassand	1987	5/52	10/55	0.48	(0.15 - 1.51)
Vlay	1988	1/13	2/12	0.42	(0.03 - 5.30)
Kennedy	1988	12/191	17/177	0.63	(0.29 - 1.36)
ISIS-2	1988	791/8592	1029/8595	0.75	(0.68 - 0.82)
Pooled summary				**0.76**	**(0.67 - 0.85)**

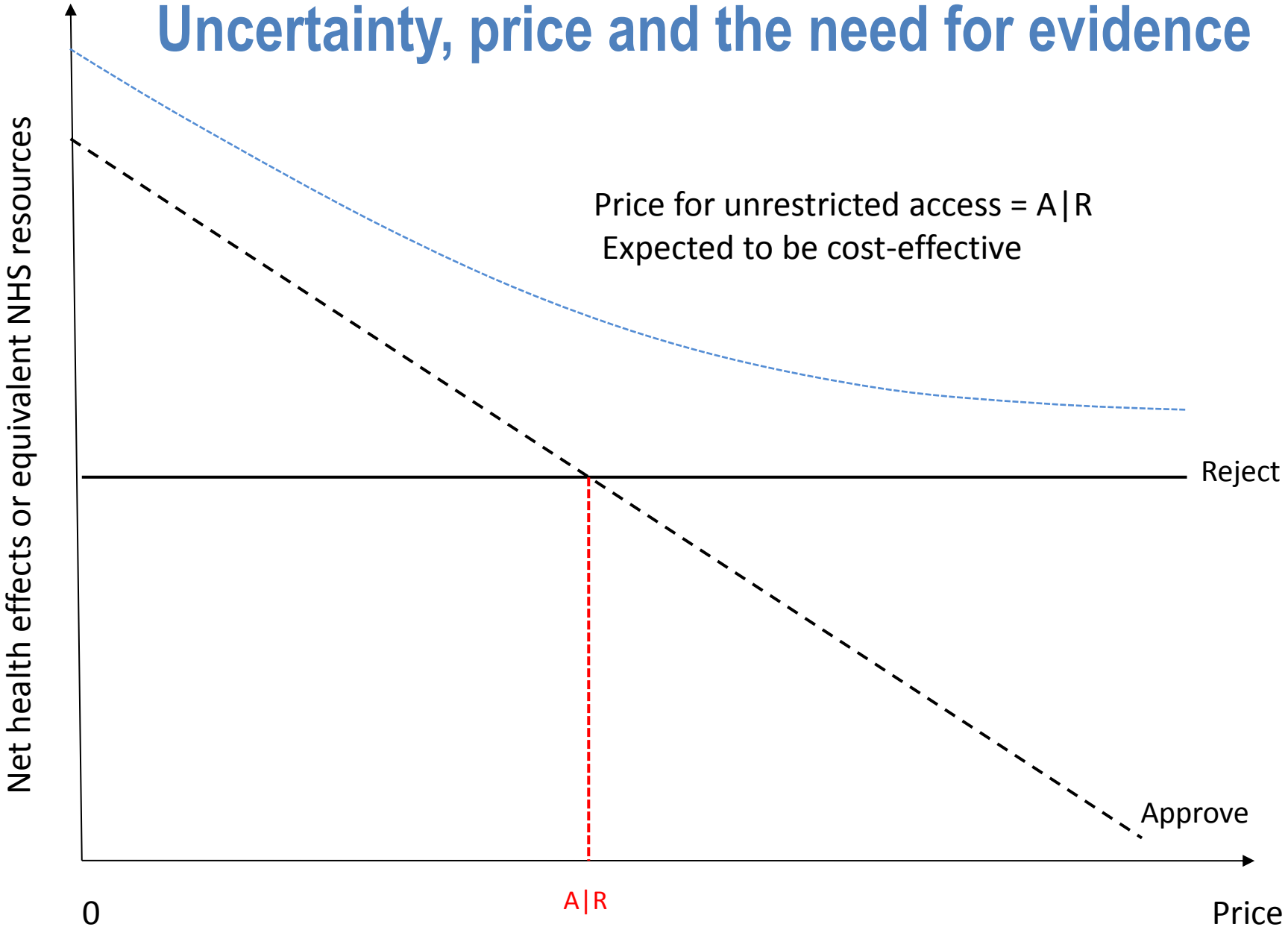


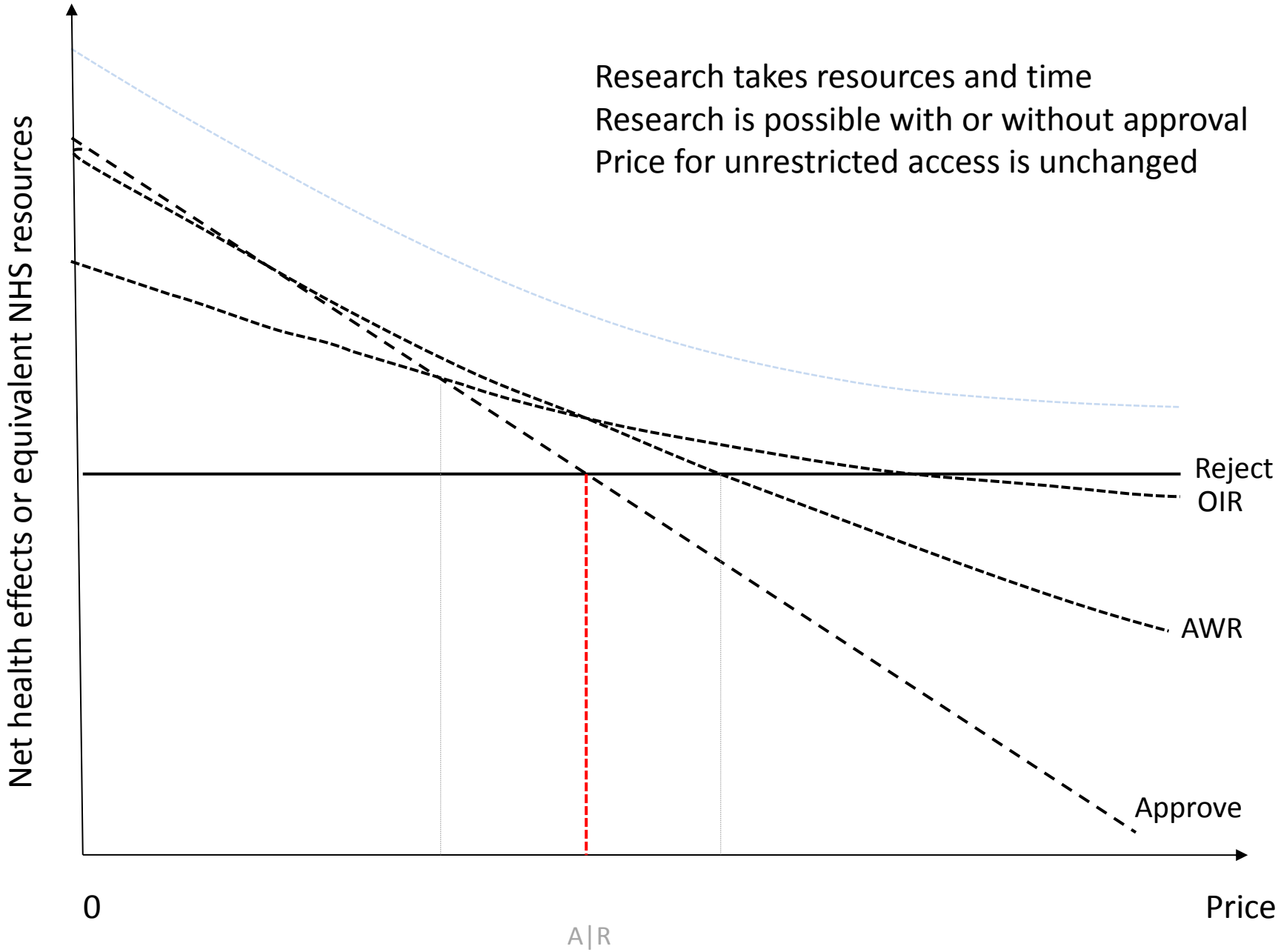


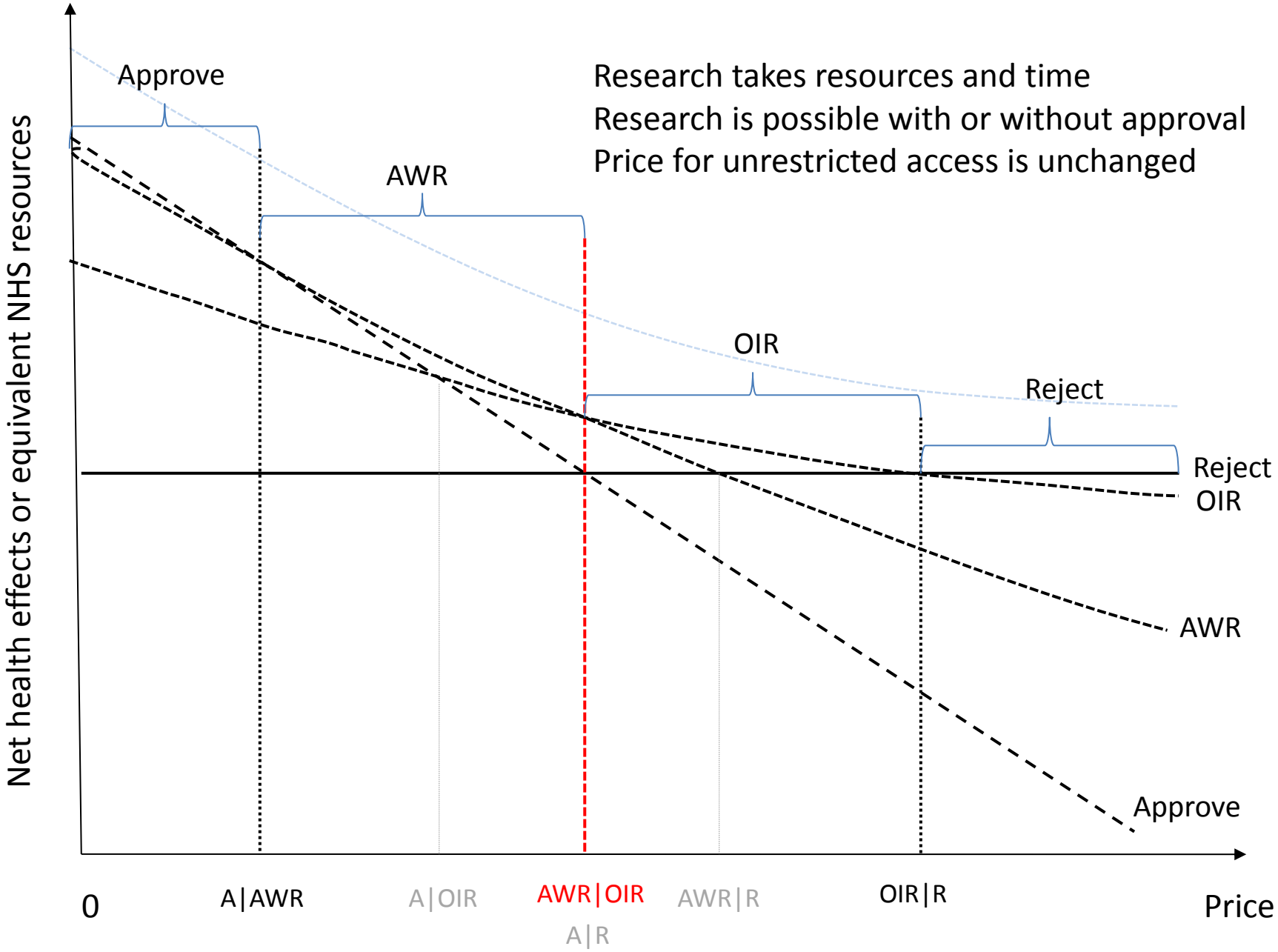
Value of implementation and the value of information

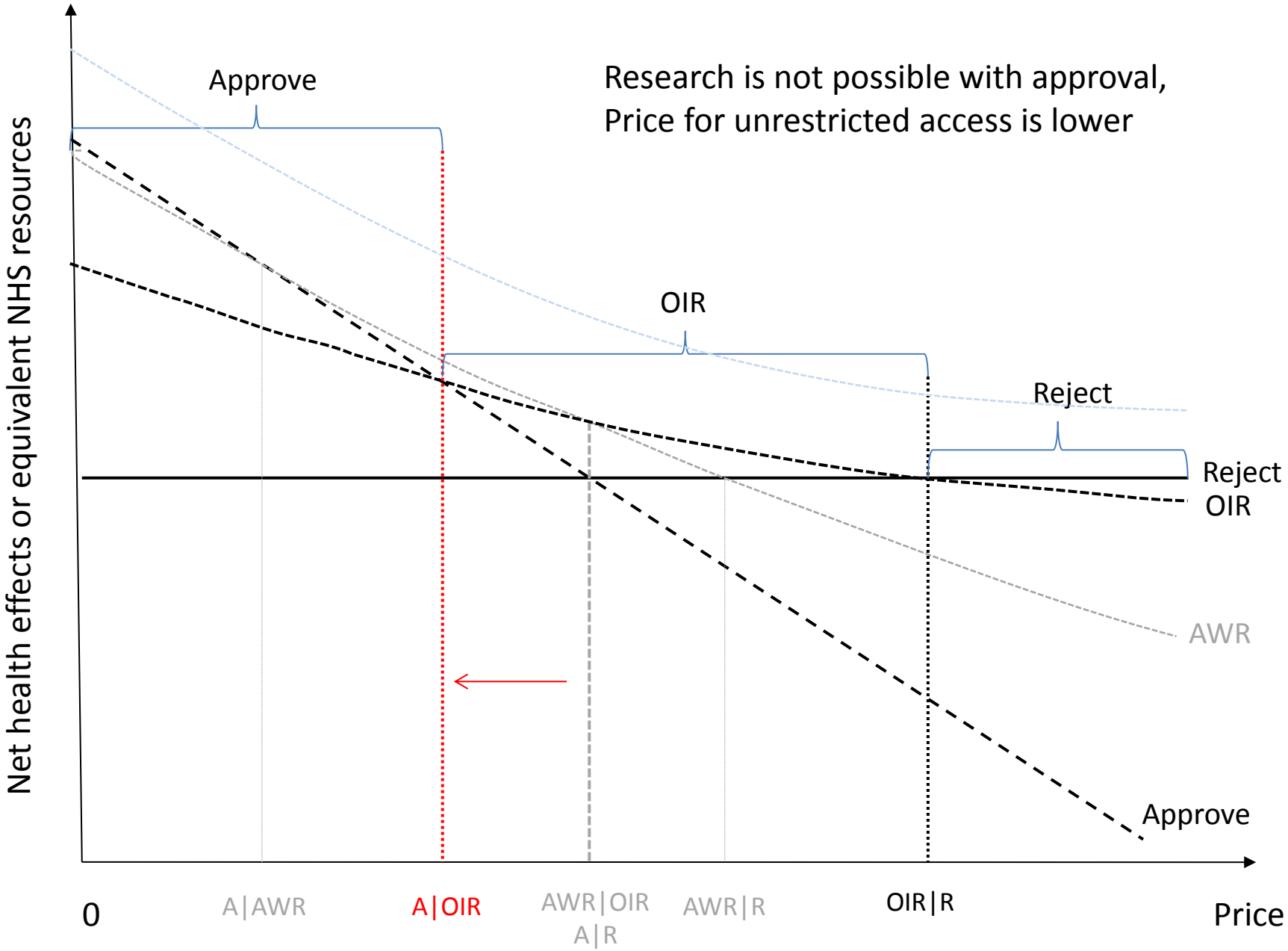


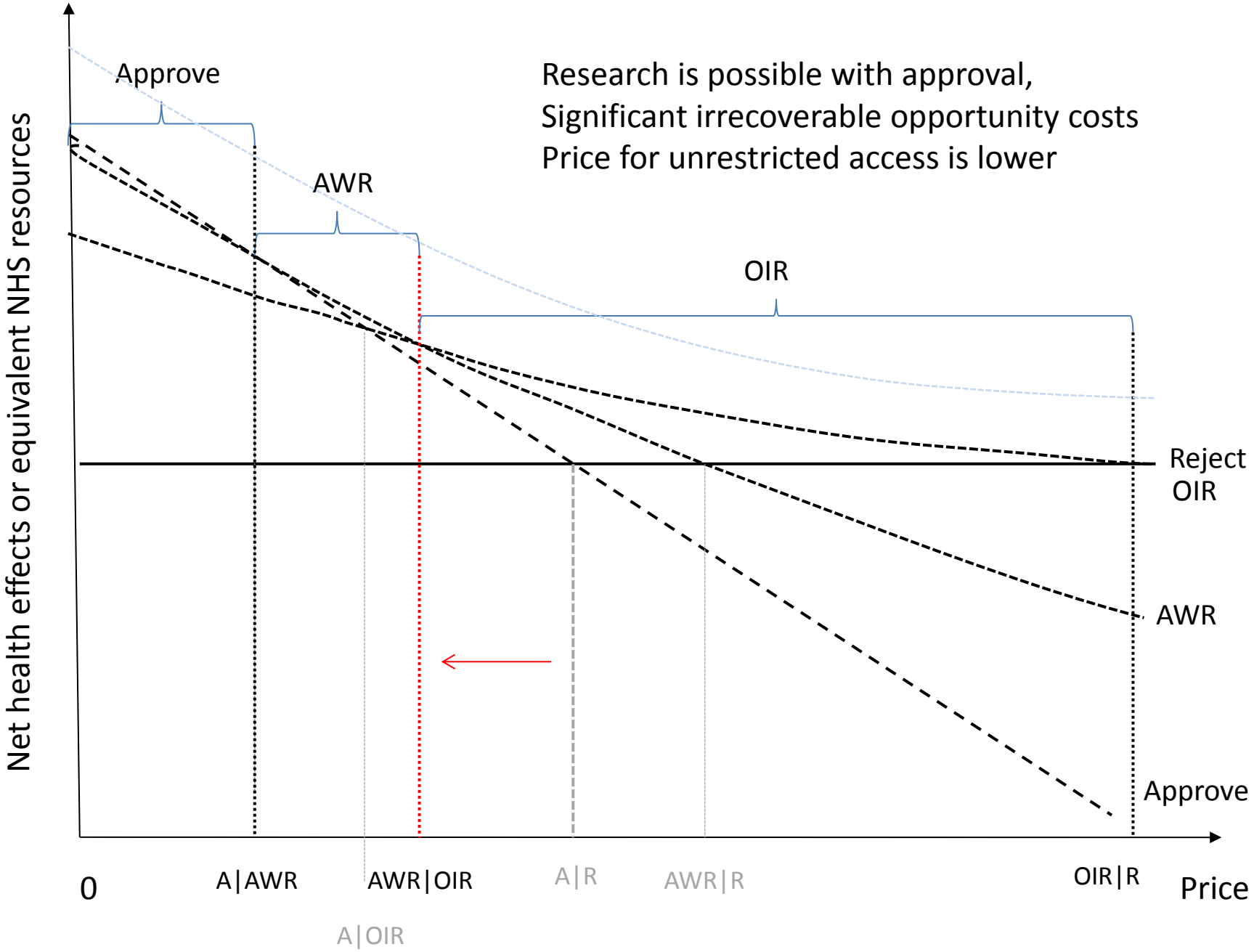
Uncertainty, price and the need for evidence




Research takes resources and time
Research is possible with or without approval
Price for unrestricted access is unchanged
Net health effects or equivalent NHS resources
Reject
OIR
AWR
Approve
0
Price


Approve
AWR
OIR
Reject
Reject
OIR
AWR
Approve
Research takes resources and time
Research is possible with or without approval
Price for unrestricted access is unchanged
Net health effects or equivalent NHS resources
0
A|AWR
A|OIR
AWR|OIR
A|R
AWR|R
OIR|R
Price


Net health effects or equivalent NHS resources
Approve
Research is not possible with approval,
Price for unrestricted access is lower
OIR
Reject
Reject
OIR
AWR
Approve
0
A|AWR
A|OIR
AWR|OIR
A|R
AWR|R
OIR|R
Price


Approve
AWR
OIR
Research is possible with approval,
Significant irrecoverable opportunity costs
Price for unrestricted access is lower
Net health effects or equivalent NHS resources
Reject OIR
AWR
Approve
0
A|AWR
AWR|OIR
A|R
AWR|R
OIR|R
Price
A|OIR

Implications

- Price for unrestricted access
  - Commonly lower but rarely higher
- Prices renegotiated once research reports:
  - Manufacturers get all the value of the research
  - HCS only benefits from research when patent expires
  - Only value if uncertain at generic prices
- Prices not renegotiated:
  - HCS get all the value of the research
- Informs who should pay for or conduct the research

Some reading

Brouwer W., Culyer AJ., Job N., van Exel A. and Rutten FH. Welfarism vs. extra-welfarism. Journal of Health Economics 2008; 27: 325-338.

Claxton K, Paulden M, Gravelle H, Bouwer W and Culyer AJ. Discounting and decision making in the economic evaluation of health care technologies. Health Economics 2011; 20: 2-15.

Claxton K, Asaria M, Chansa C, Jamison J, Lomas J, Ochalek J et al. Accounting for Timing when Assessing Health-Related Policies. Journal of Benefit-Cost Analysis. 2019 Jan 26.

Claxton K., Griffin S., Koffijberg H. and McKenna C.How to estimate the health benefits of additional research and changing clinical practice. British Medical Journal. 2015; 351:1-5.

Drummond MF., Sculpher MJ., Claxton K., Stoddart GL. and Torrance GW (2015), Methods for the economic evaluation of health care programmes (4th edition), Oxford Medical Publications. Chapters 2, 4 and 11

Espinoza, M.A., Manca, M., Claxton, K., et al. The value of heterogeneity for cost-effectiveness subgroup analysis: conceptual framework and application. Medical Decision Making. 2014; 34: 951–64.

Griffin S. Claxton K., Palmer S. and Sculpher MJ. Dangerous Omissions: The consequences of ignoring decision uncertainty. Health Economics 2011;20:212-24.

Lomas JRS, Martin S, Claxton KP. Estimating the marginal productivity of the English National Health Service from 2003 to 2012. Value in Health. 2019 Sep;22(9):995-1002.

McKenna C, Soares M, Claxton K, Bojke L, Griffin S, Palmer S et al. Unifying Research and Reimbursement Decisions: Case Studies Demonstrating the Sequence of Assessment and Judgments Required. Value in health. 2015 Sep;18(6):865-875.

Some reading

Nord, E. (2011). Discounting future health benefits: the poverty of consistency arguments. Health Economics, 20, 16–26.

Ochalek JM, Lomas JRS, Claxton KP. Estimating health opportunity costs in low- and middle-income countries: a novel approach and evidence from cross-country data. BMJ Global health. 2018 Sep 15

Ochalek J, Revill P, Manthalu G, McGuire F, Nkhoma D, Rollinger A et al. Supporting the development of a health benefits package in Malawi. BMJ Global health. 2018 Apr 9;3(2).

Paulden M, and Claxton K. Budget allocation and the revealed social rate of time preference for health. Health Economics 2011; 21: 612–618.

Woods B, Revill P, Sculpher M, Claxton K. Country-Level Cost-Effectiveness Thresholds: Initial Estimates and the Need for Further Research. Value in Health. 2016 Dec 14;19(8):929-935