Methods for the Estimation of the NICE Cost Effectiveness Threshold

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What do we need?

- Compare
  - Health *expected* to be gained
  - Health *expected* to be lost due to additional NHS costs
- Expected health effects of changes in NHS expenditure
- What its not
  - Consumption value of health (willingness to pay)
  - Marginal productivity of 'ideal' NHS
- No simple relationship with changes in
  - Budget, prices and productivity
  - Health production outside NHS

How can we estimate it?

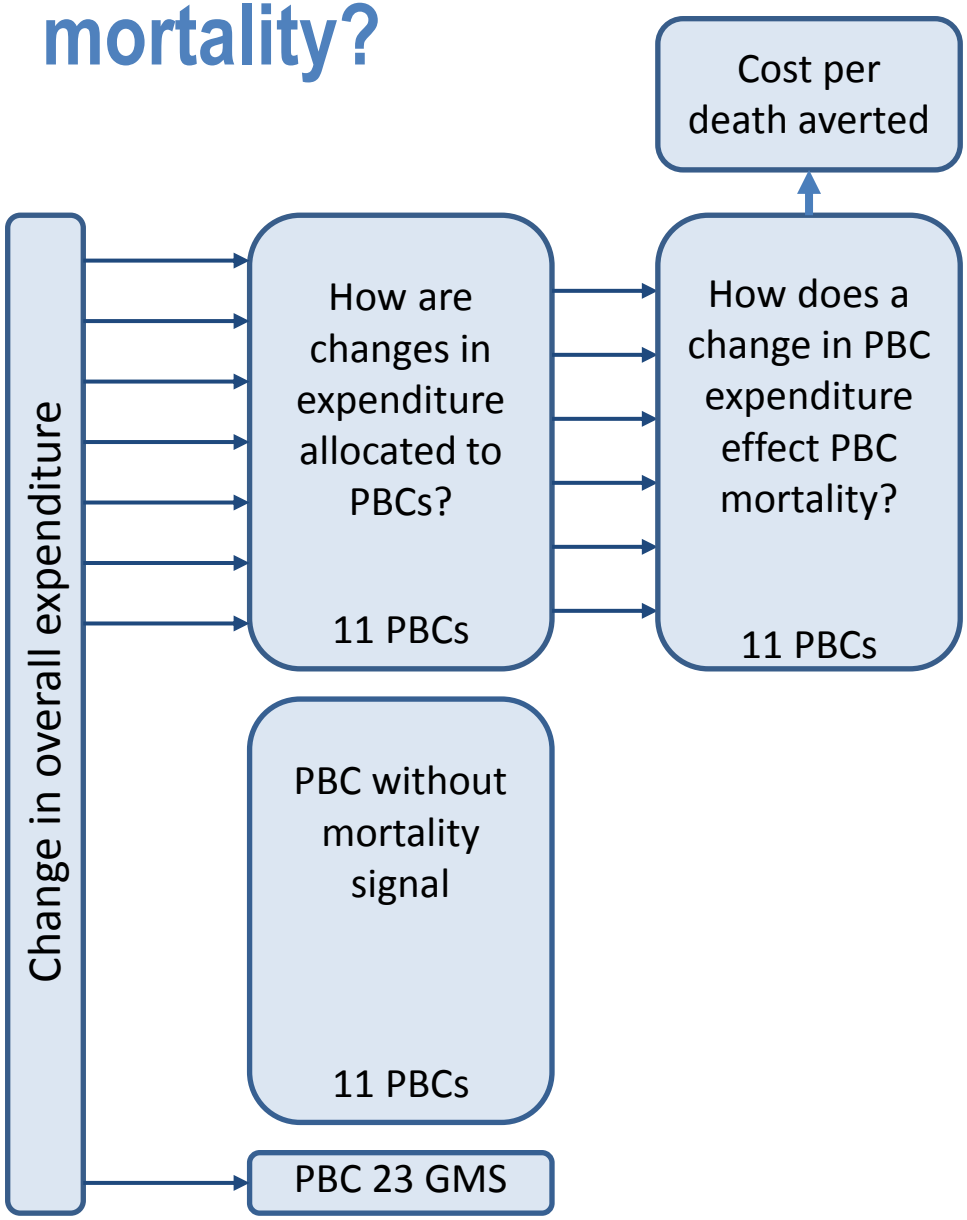
- Implied value from past decisions based on informal judgements — NICE threshold Range 2004 (2001)
- Find out what decisions are made and estimate impact on cost and health — Appleby et al 2007
- Estimate the relationship between changes in expenditure and outcomes — Martin et al 2008, 2009
  - 23 Programme Budget Categories (PBCs)
    - Disease areas (groups of ICD codes)
    - All expenditure allocated to each PBC
  - 152 Primary Care Trusts (PCTs)
    - Local areas of the NHS
    - Mortality within each PBC

How can we estimate effects of expenditure on mortality (deaths)?

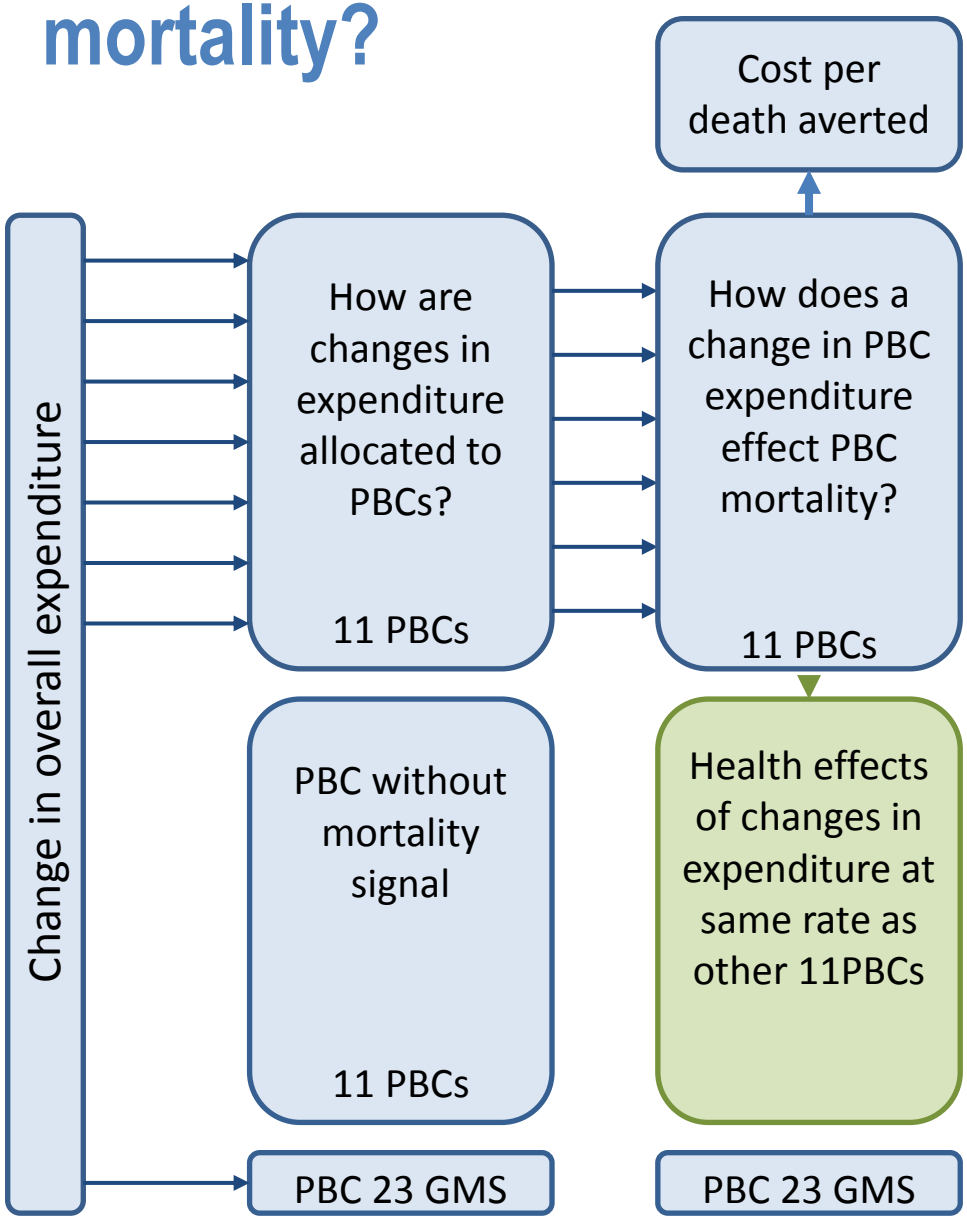
- Change in PBC expenditure due to change in overall expenditure
  - Differences in spend on a particular PBC and total spend across PCTs
  - Account for other reasons why PBC spend might differ between PCTs
  - Isolate the effects on PBC spend of changes in overall expenditure

- Change in PBC mortality (deaths) due to change in PBC expenditure
  - Differences in PBC mortality and PBC expenditure across PCTs
  - Account for other reasons why PBC mortality might differ between PCTs
  - Isolate the effects on PBC mortality of changes in PBC expenditure

How can we estimate effects of expenditure on mortality?



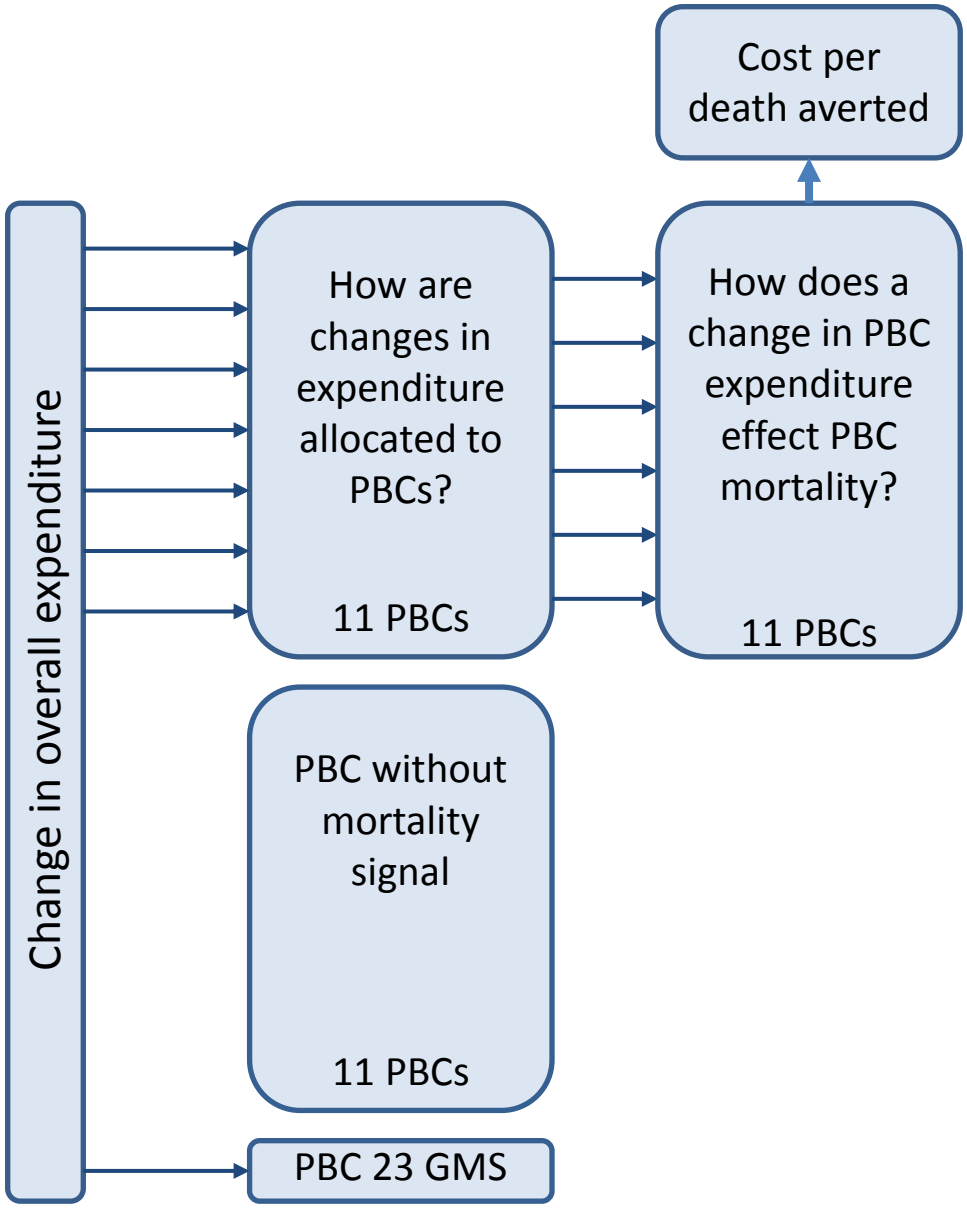
How can we estimate effects of expenditure on mortality?



Estimates of the threshold (2008-09)

	Cost per death averted
QoI associated with LYs	-
QoI during disease	-
YLL per death averted	-
QALYs per death averted	-
11 PBCs (with mortality)	£105,872
All 23 PBCs	£114,272

How can we estimate effects on life years



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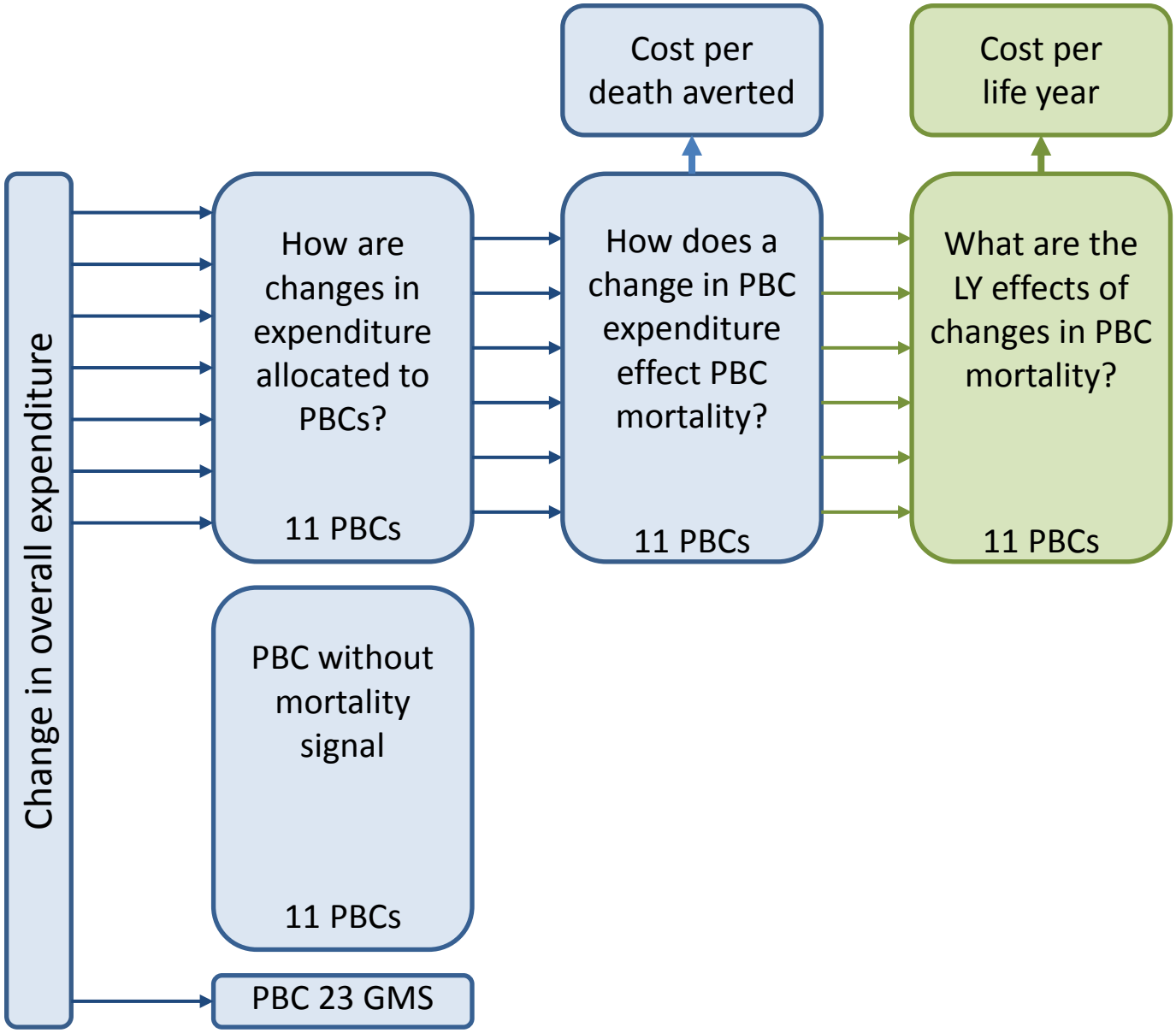

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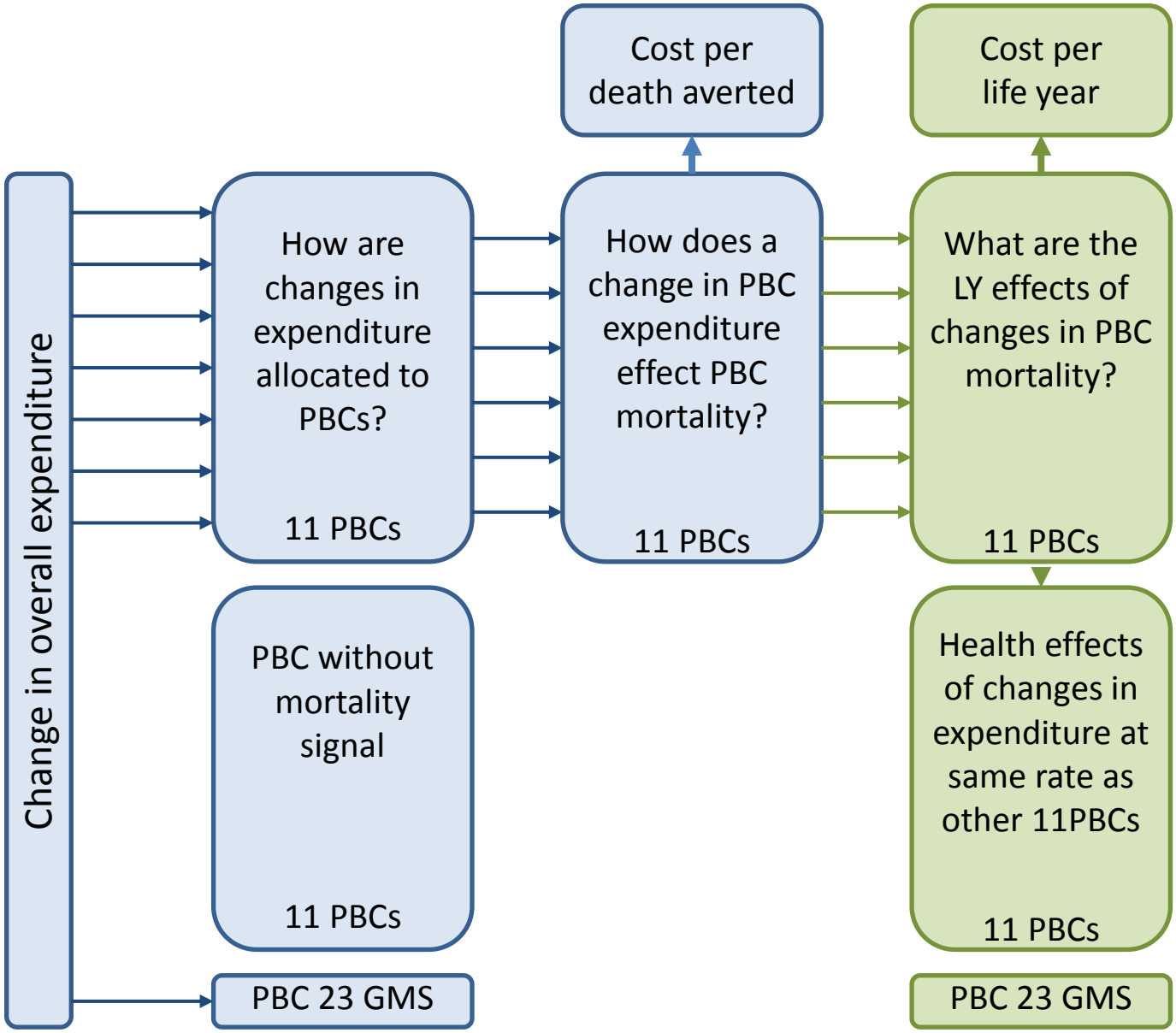


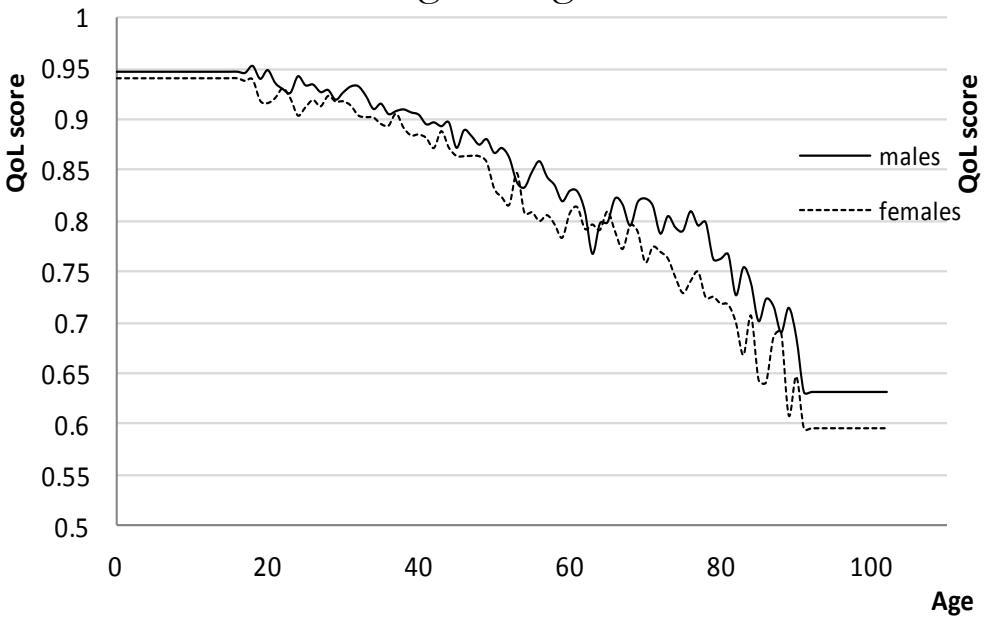
Estimates of the threshold (2008-09)

	Cost per death averted	Cost per life year
QoI associated with LYs	-	*1*
QoI during disease	-	*0*
YLL per death averted	-	*4.5 YLL*
QALYs per death averted	-	*4.5 YLL*
11 PBCs (with mortality)	£105,872	£23,360
All 23 PBCs	£114,272	**£25,214**

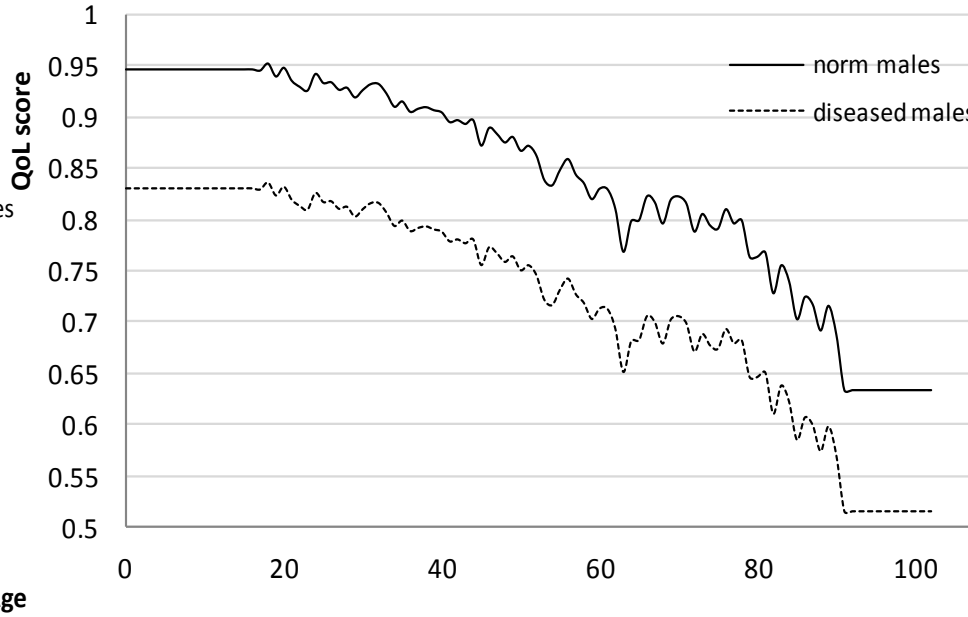
How can we adjust life years for quality?

- Life years lived at QoI norms by age and gender
  - All disease is acute *or* symptoms are 'curable'
- Life years lived with QoI of disease (decrement to norms)
  - All disease is chronic (life long) *and* 'incurable'
- Assumptions are relaxed using measures of burden

Quality of life for the general population by age and gender



Quality of life for males in PBC1 (infectious disease



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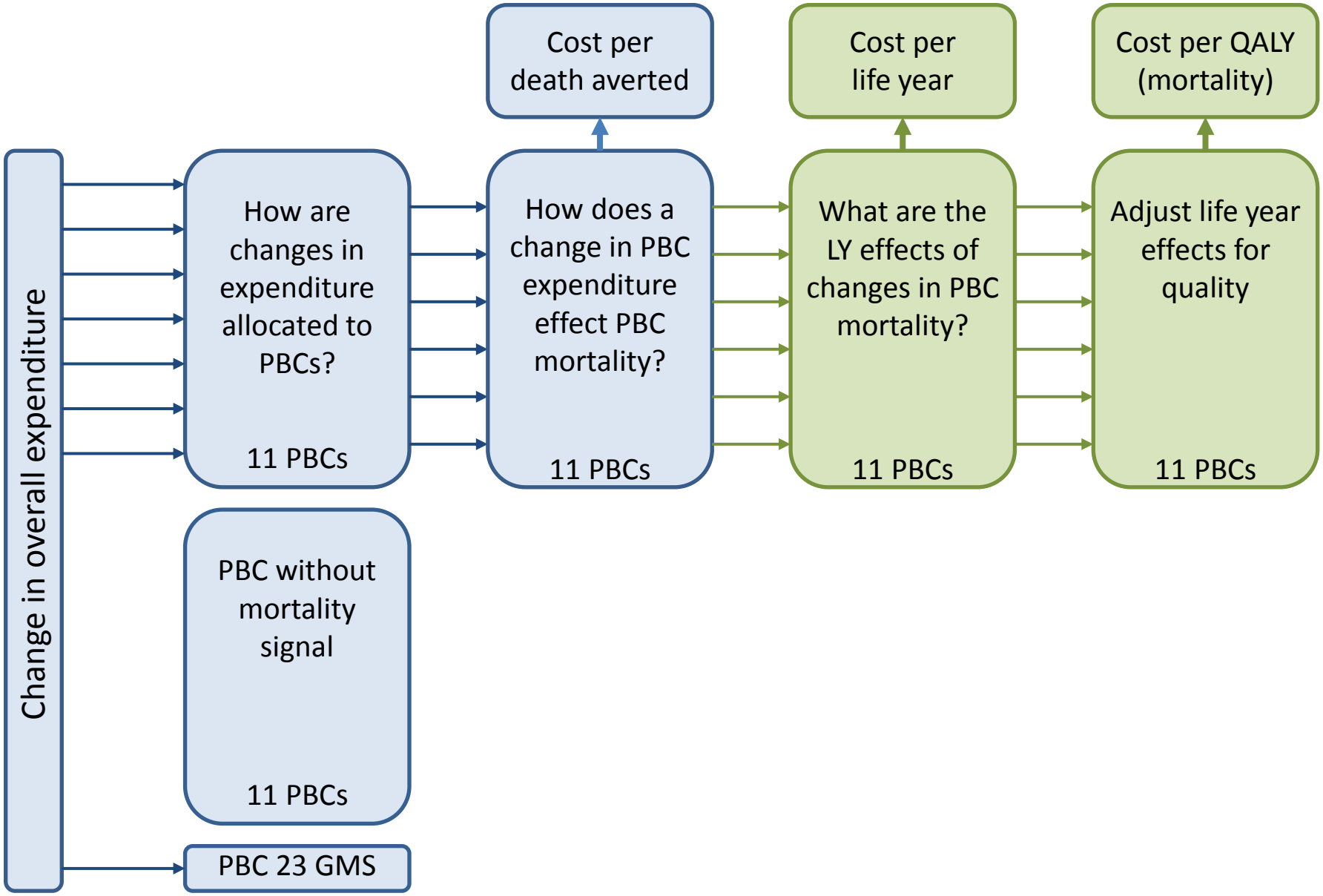

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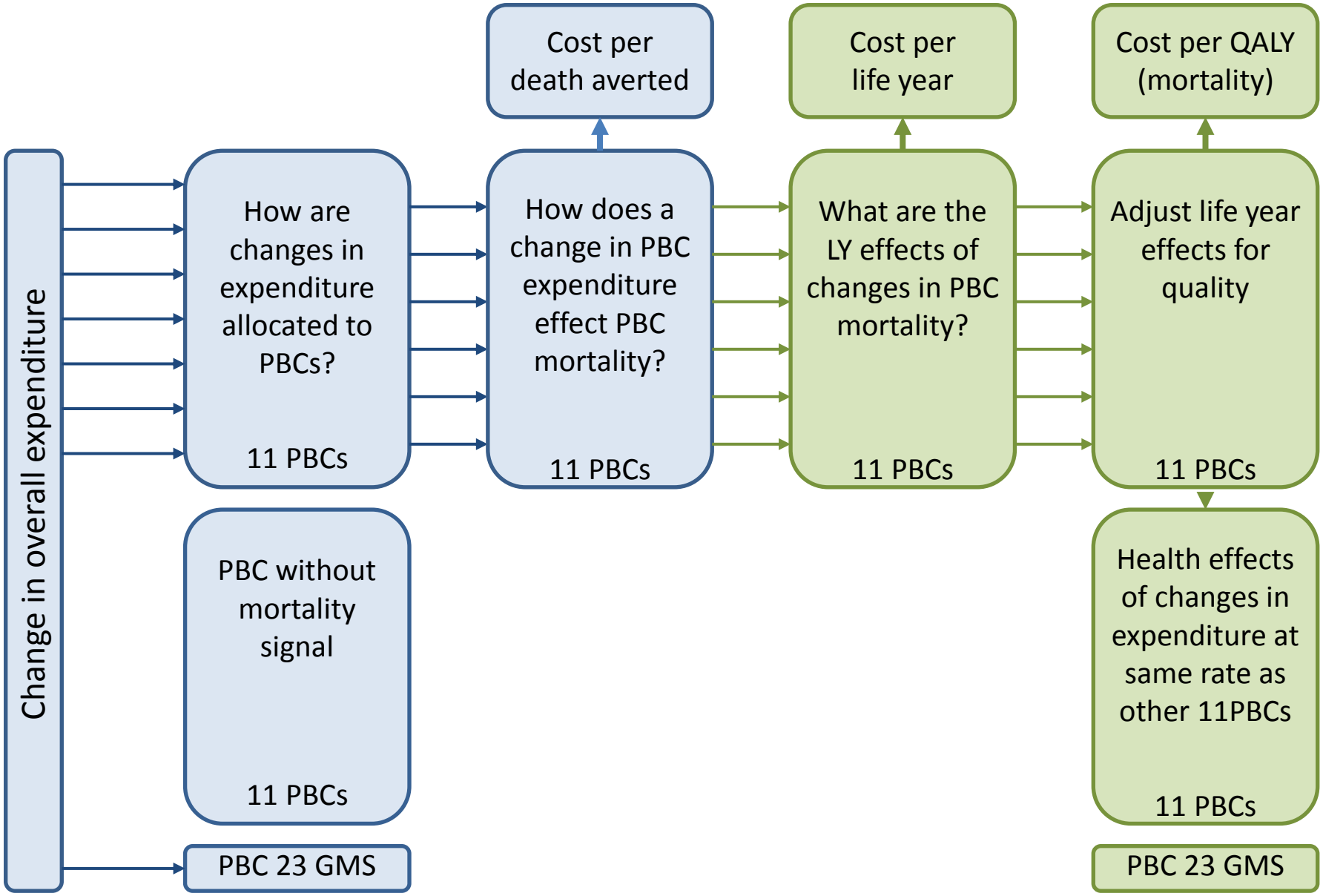

Estimates of the threshold (2008-09)

	Cost per death averted	Cost per life year	Cost per QALY (mortality effects only)	
QoI associated with LYs	-	*1*	*Norms*	*Disease*
QoI during disease	-	*0*	*0*	*0*
YLL per death averted	-	*4.5 YLL*	*4.5 YLL*	*4.5 YLL*
QALYs per death averted	-	*4.5 YLL*	*3.8 QALY*	*3.0 QALY*
11PBCs (with mortality)	£105,872	£23,360	£28,045	£35,397
All 23 PBCs	£114,272	£25,214	**£30,270**	£38,206

How can we account for possible effects on quality of life?

- No observations of quality life by PBC at PCT level
  - Quality of life is important in 11 PBCs with mortality
  - Mortality is (almost) irrelevant in the other 11 PBCs
  - Much NHS activity is primarily to improve quality of life
- Possible responses
  - Assume that NHS expenditure has no effects on quality of life
  - Surrogacy
    - Proportionate effect mortality burden used as surrogate for QoI effects
  - Extrapolation
    - Proportionate effect on QALY burden is similar in the other 11 PBCs
  - Use what can be observed to impute what cannot

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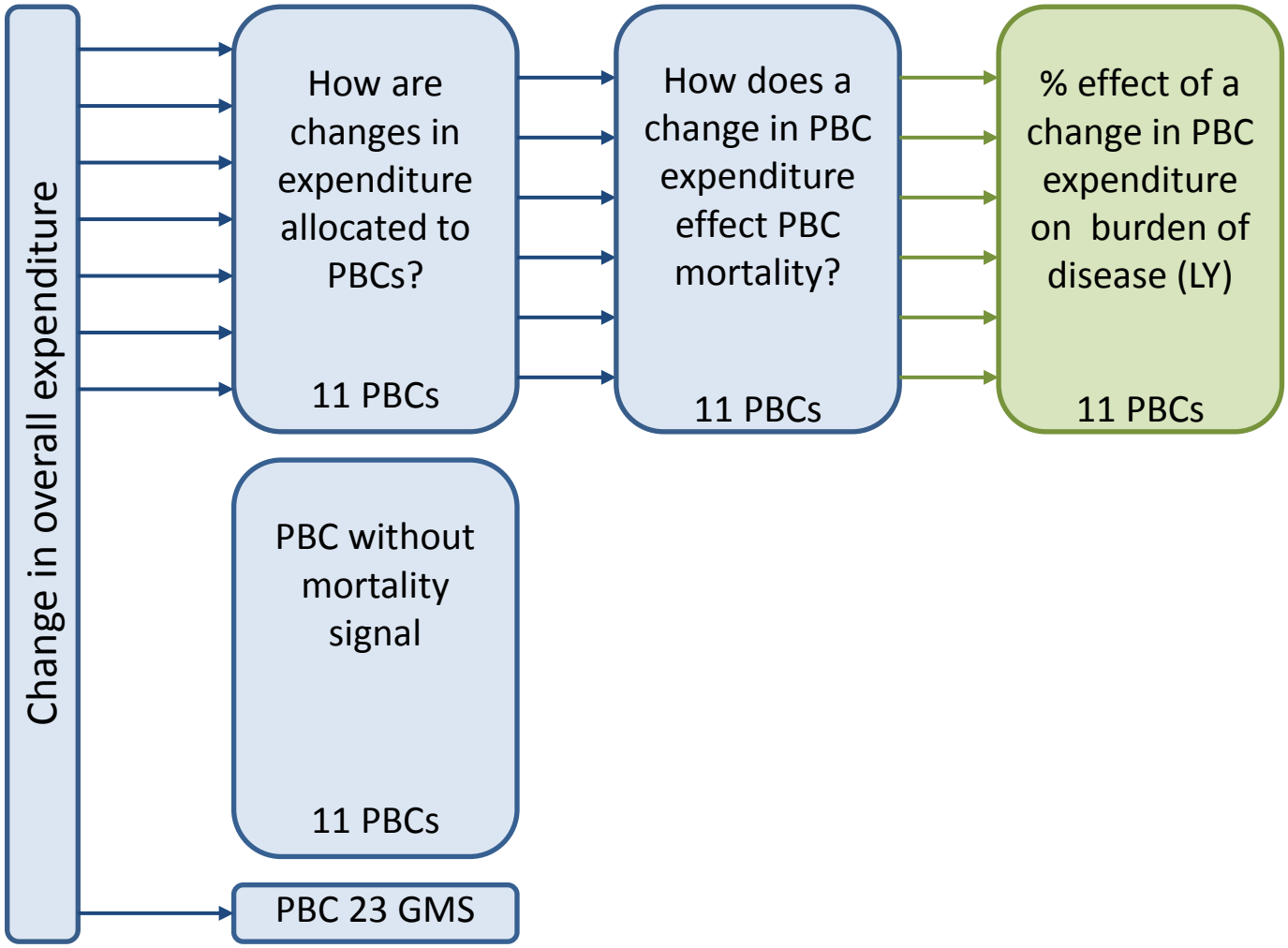

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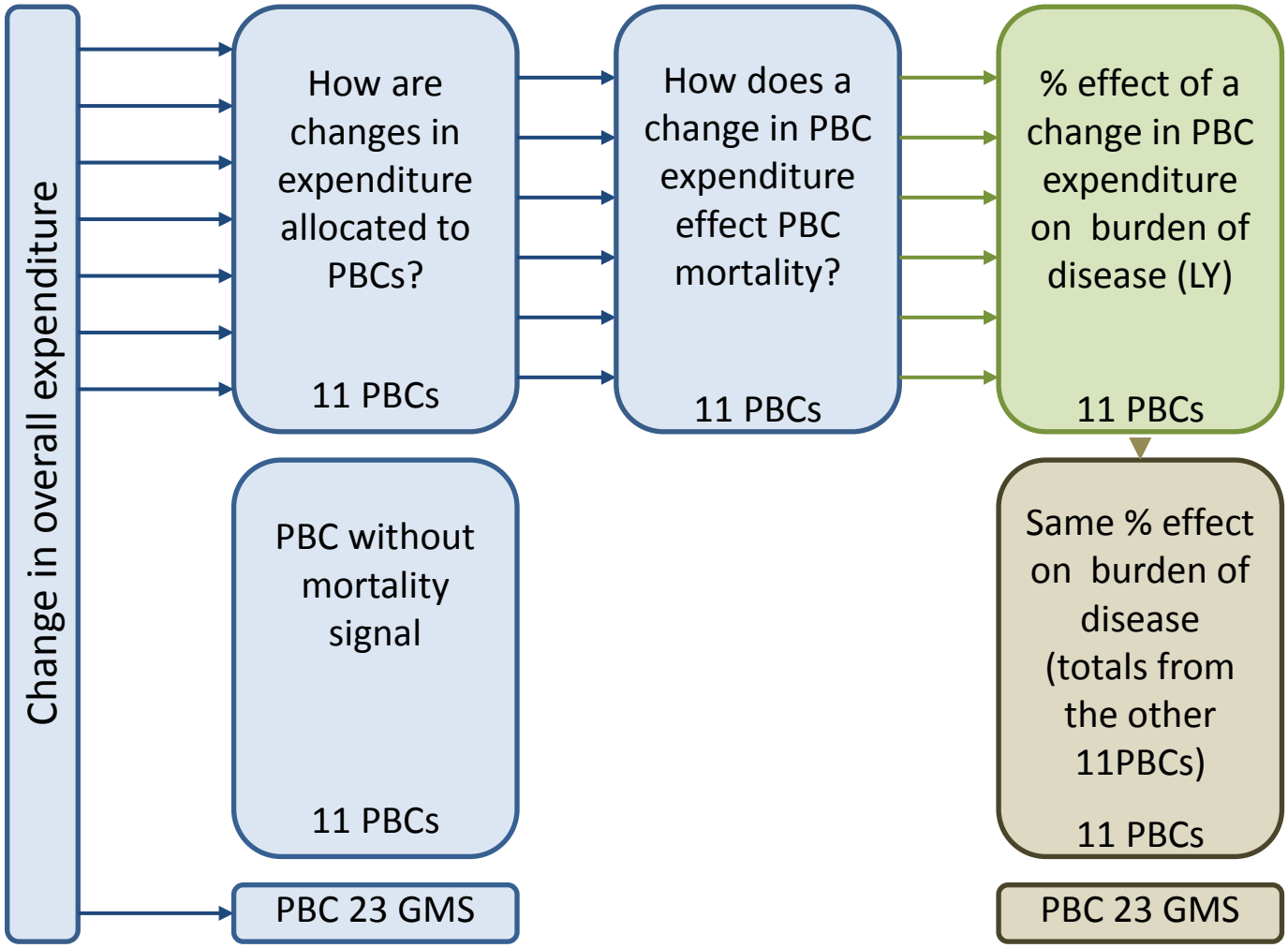

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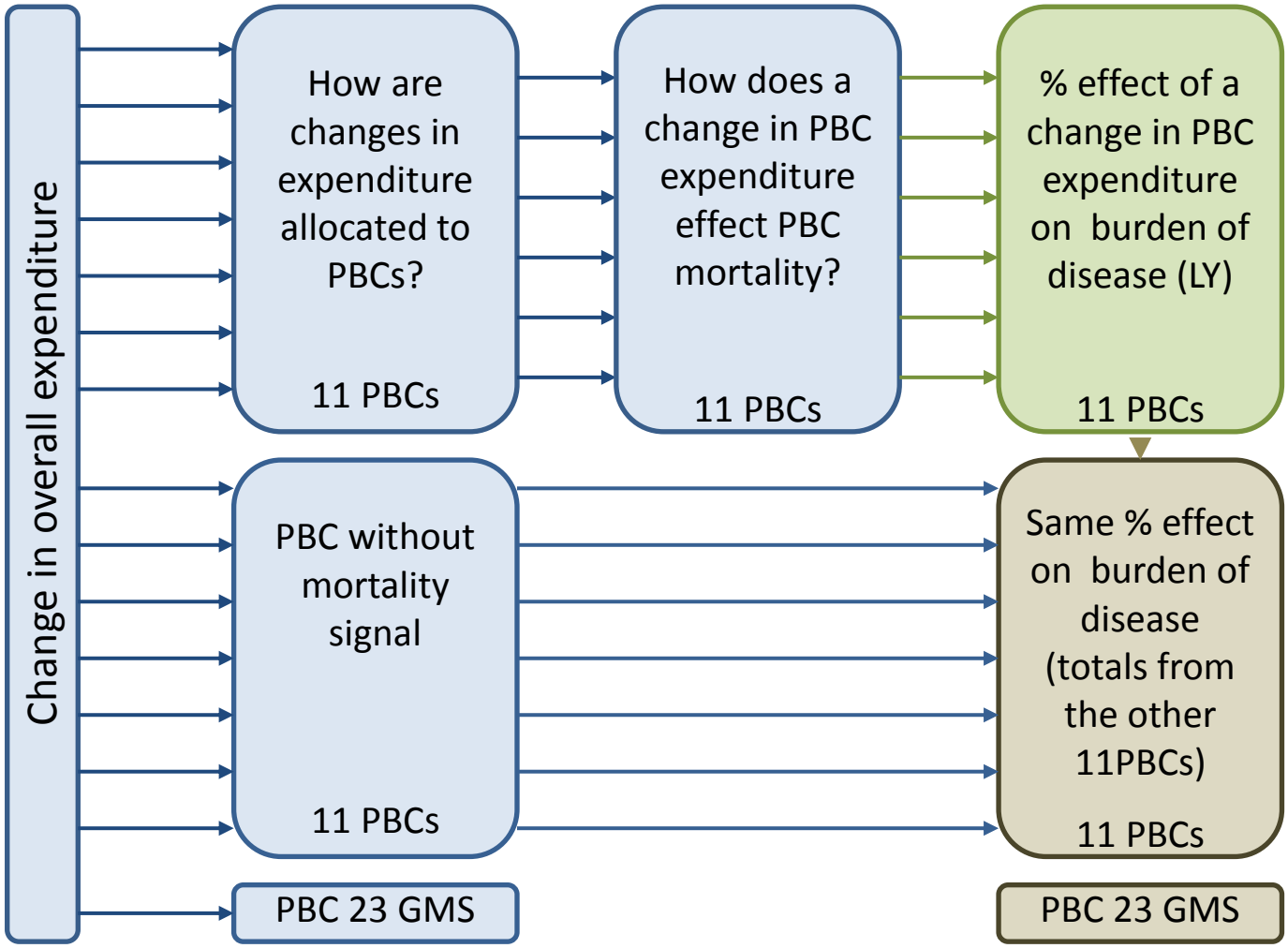

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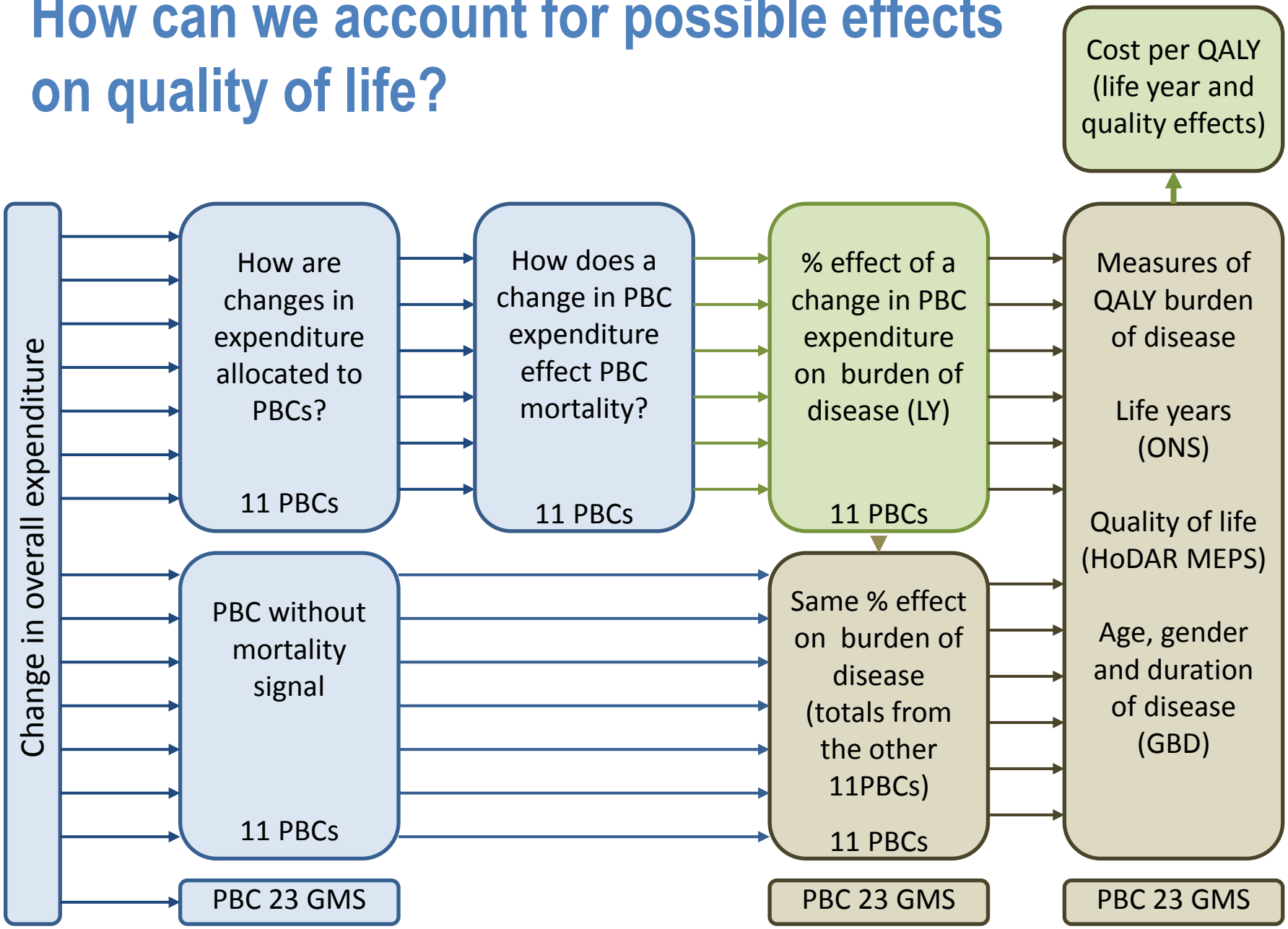


Estimates of the threshold (2008-09)

	Cost per death averted	Cost per life year	Cost per QALY (mortality effects)	Cost per QALY
QoI associated with LYs	-	*1*	*Norms*	*Based on burden*
QoI during disease	-	*0*	*0*	*Based on burden*
YLL per death averted	-	*4.5 YLL*	*4.5 YLL*	*4.5 YLL*
QALYs per death averted	-	*4.5 YLL*	*3.8 QALY*	*12.7 QALY*
11 PBCs (with mortality)	£105,872	£23,360	£28,045	£8,308
All 23 PBCs	£114,272	£25,214	£30,270	**£12,936**

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

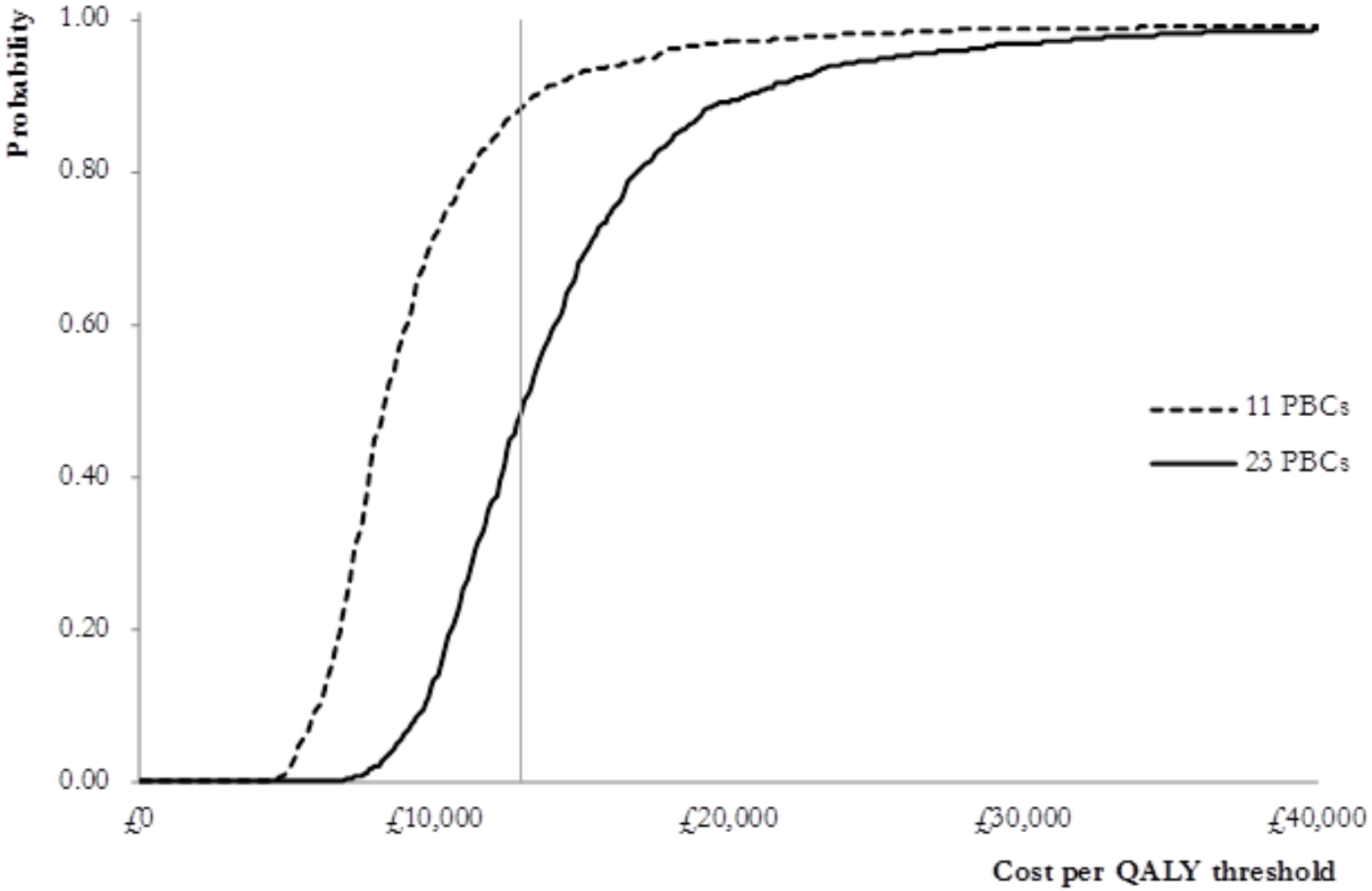
Which PBCs matter most?

PBC	% spend	% health	Elasticity	PBC cost per QALY
Cancer	4.47	3.41	0.34	£16,997
Circulatory	7.59	13.95	1.40	£7,038
Respiratory	4.58	29.67	2.97	£1,998
Gastro-intestinal	3.20	5.68	0.57	£7,293
Infectious diseases	3.27	2.03	0.20	£20,829
Endocrine	1.89	7.84	0.78	£3,124
Neurological	5.98	14.11	1.41	£5,480
Genito-urinary	4.64	1.37	0.14	£43,813
Trauma & injuries*	7.70	0	0	NA
Maternity & neonates*	6.83	0.03	<0.01	£2,969,208
Disorders of Blood	2.06	2.82	0.28	£9,419
Mental Health	17.86	12.32	1.23	£18,744
Learning Disability	1.04	0.09	0.01	£149,883
Problems of Vision	1.94	0.55	0.05	£45,788
Problems of Hearing	0.87	1.81	0.18	£6,239
Dental problems	2.89	0.88	0.09	£42,472
Skin	1.97	0.25	0.03	£101,042
Musculo skeletal	3.63	3.00	0.30	£15,628
Poisoning and AE	0.93	0.11	0.01	£113,546
Healthy Individuals	3.53	0.09	0.01	£526,771
Social Care Needs	3.00	0	0	NA
Other	10.14	0	0	NA

How uncertain are the estimates?

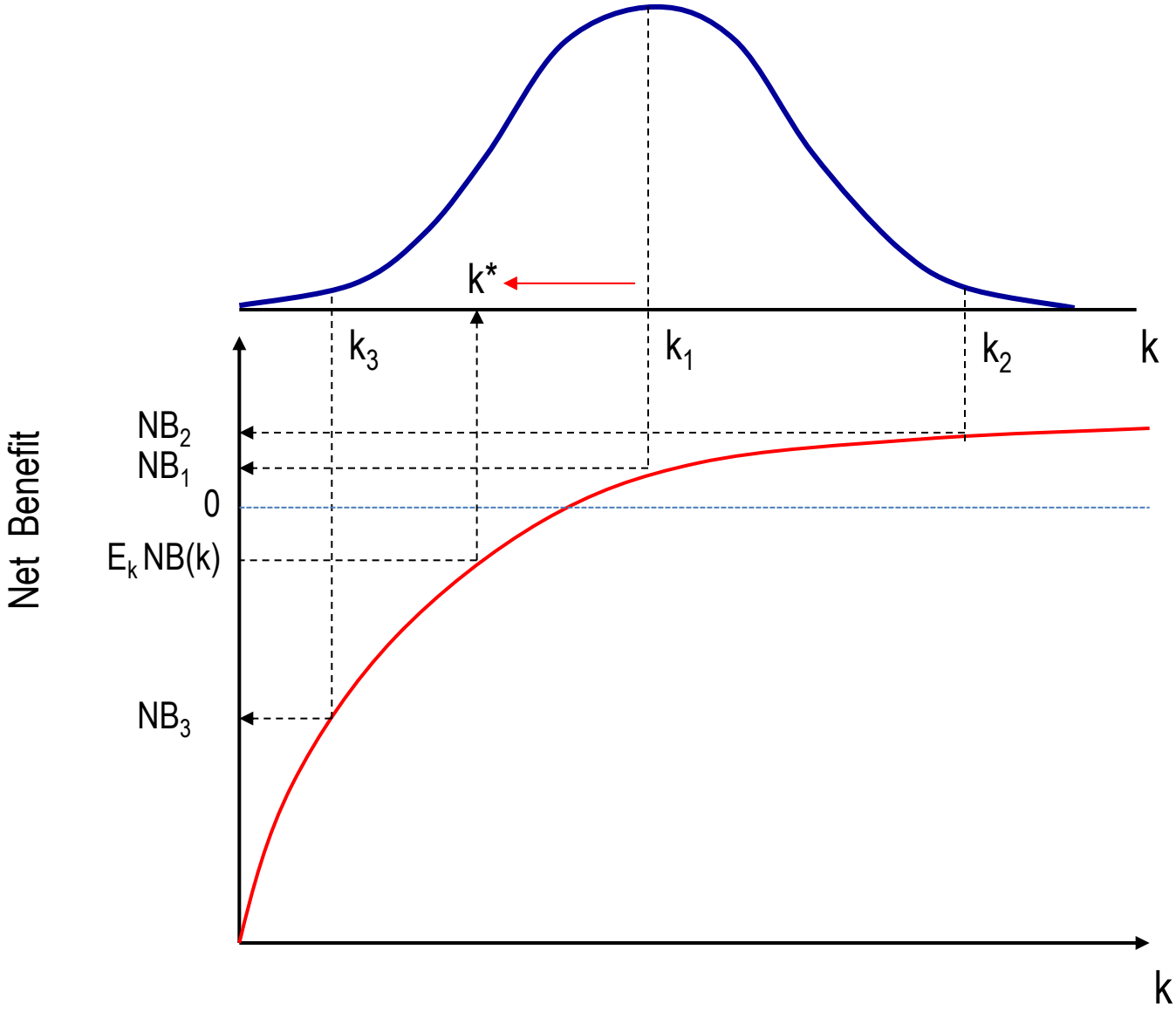
An assessment of parameter uncertainty

Figure 5.1 Cumulative probability density function for the cost per QALY threshold



Implications of uncertainty in the estimate

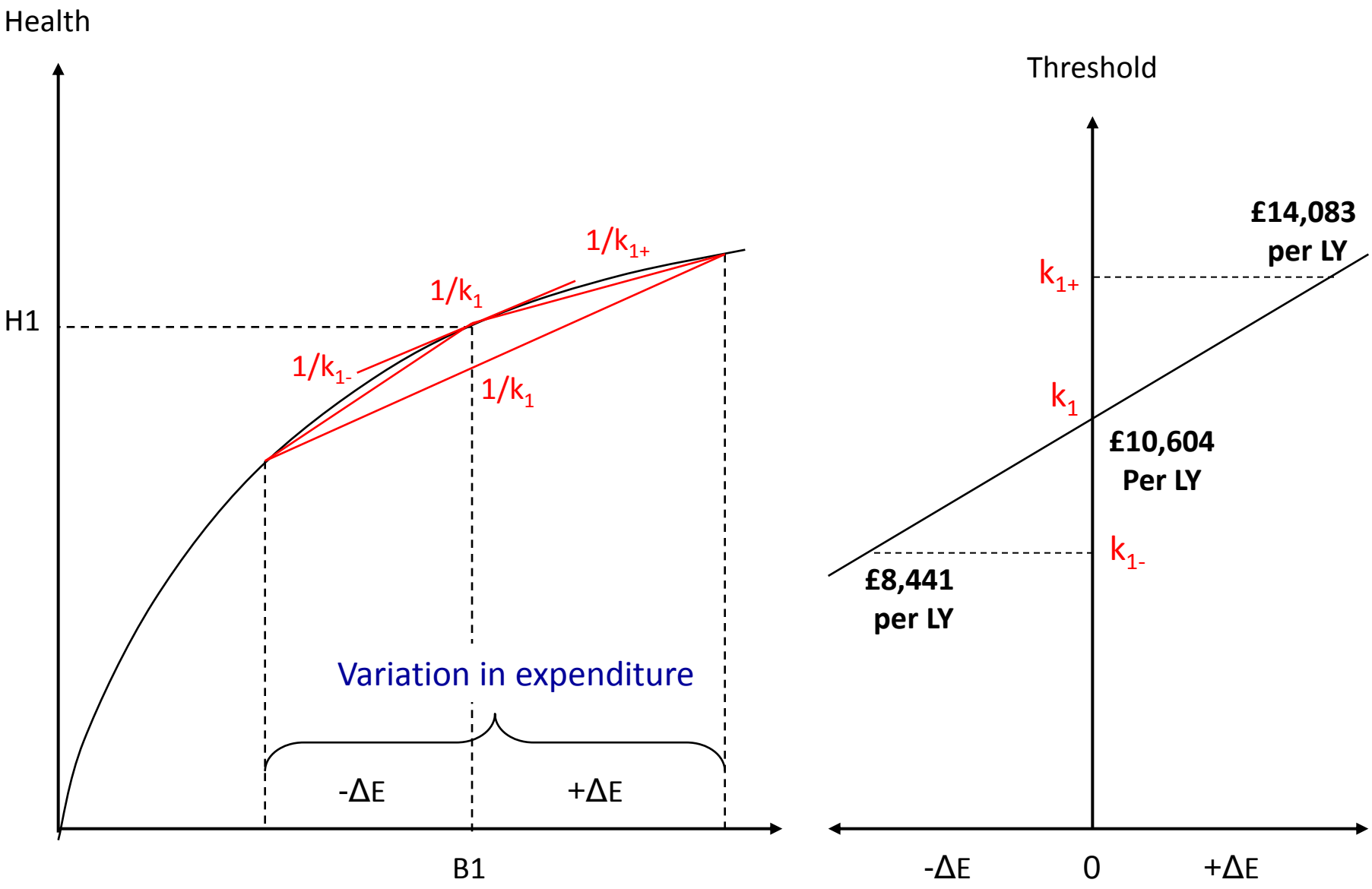
(Single threshold value that can be compared to an ICER)



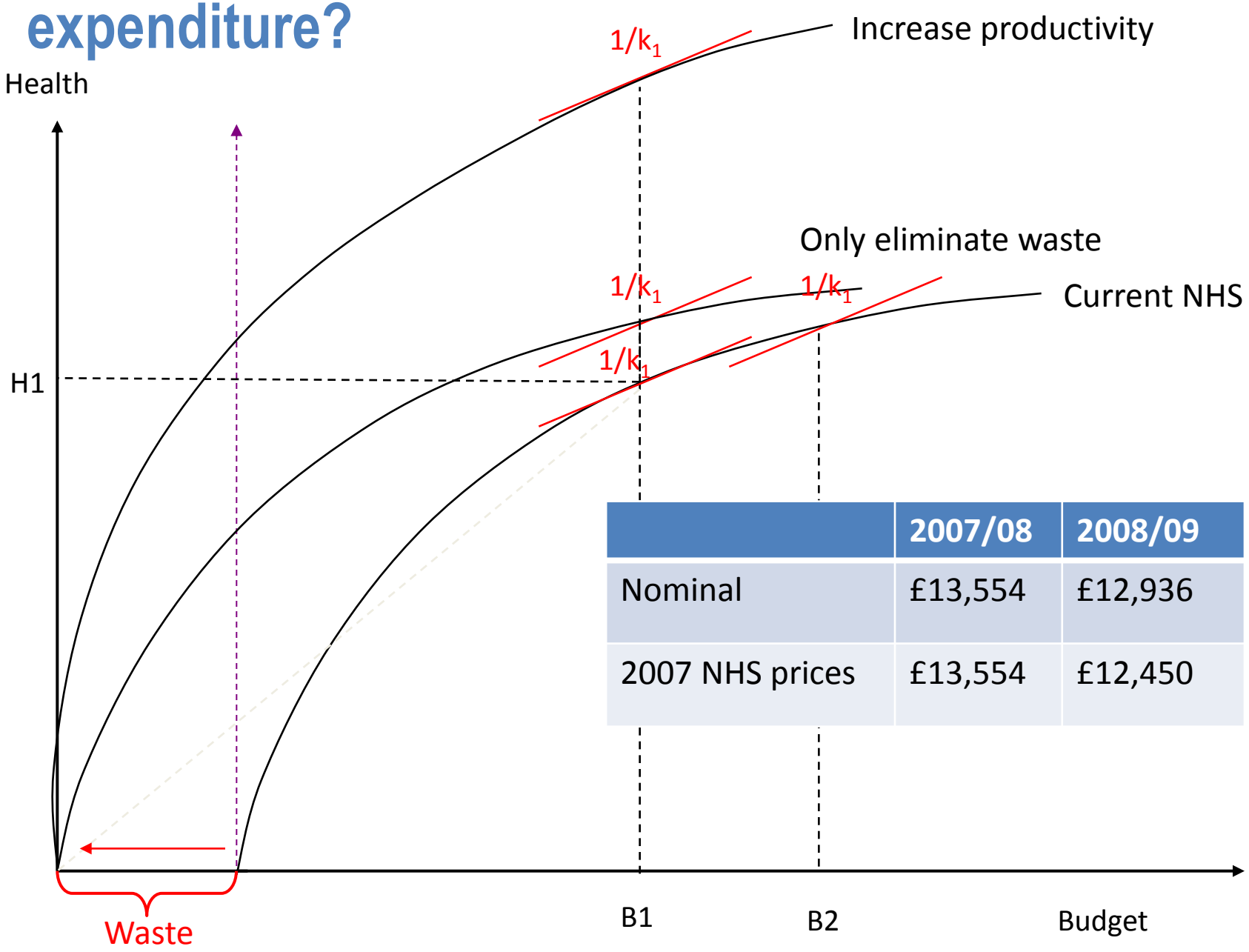
Is it likely to be an under or over estimate?

- Health effects over estimated (threshold underestimated)?
  - Deaths averted returns the individuals to the mortality risk of the general population (matched for age and gender)
  - Small positive correlation between expenditure and outcome elasticities
  - Apply estimates (data reported at PCT) to all PBC mortality
- Health effects under estimated (threshold overestimated)?
  - Mortality and quality of life effects restricted to one year
  - No effects of prevention (reduce incidence into the at risk population)
  - Effects of changes in GMS (and PBC22 & 16) expenditure not fully captured
- Other assumptions
  - Surrogacy
    - Are % mortality effects a good surrogate for % QoI effects?
  - Extrapolation
    - Is the proportionate effect on QALY burden of changes in spend similar in the other PBCs (e.g., Mental Health)?

Impact of investment and disinvestment?



How does the threshold change with overall expenditure?



	2007/08	2008/09
Nominal	£13,554	£12,936
2007 NHS prices	£13,554	£12,450

Summary of conclusions

- Upper bound of the NICE threshold is certainly too high
- Lower bound may also be too high
- Threshold less than the mean estimate when imposing costs on the NHS (reducing expenditure)
- No evidence of growth in threshold with increases in real budget and prices
- Some evidence that threshold more likely to fall rather than rise as NHS comes under more financial pressure
- Uncertainty in the estimate suggests a policy threshold set as less than the mean estimate
- Can reflect other displaced aspects of value

Accounting for other aspects of value?

- How much and what type of health and for whom?
  - Life years and quality of life effects
  - By age, gender and ICD code
- Severity, unmet need and burden
  - Burden of disease
  - Expected QALYs without and with disease
- Wider social benefits
  - Net production effects of a change in health
  - Marketed and non market production
  - Net of marketed and non marketed consumption

Code	Disease (pharma ICDs). Cancer in blue.	Burden of Illness Absolute QALY loss
C22	Liver cancer	10.70
C25	Pancreatic cancer	9.97
C34	Lung cancer	9.68
F20	Schizophrenia	7.62
G35	Multiple sclerosis	6.18
C92	Myeloid leukaemia	6.15
G20	Parkinson's disease	4.60
C90	Myeloma	4.45
J43	Emphysema and COPD	3.80
C64	Kidney cancer	3.75
F30	Depression	3.63
M05	Rheumatoid arthritis	2.83
E11	Diabetes	2.68
displ	***(average displaced QALY)***	2.07
J45	Asthma	1.86
G30	Alzheimer's disease	1.68
F03	Dementia	1.68
G40	Epilepsy	1.32
C18	Colon cancer	1.28
I26	Embolisms, fibrillation, thrombosis	1.16
C61	Prostate cancer	1.06
I21	Acute myocardial infarction	1.00
I64	Stroke	0.83
C53	Cervical cancer	0.60
C50	Breast cancer	0.55
A40	Streptococcal septicaemia	0.38
J30	Allergic rhinitis	0.30
M81	Osteoporosis	0.28
K50	Irritable Bowel Syndrome	0.26
J10	Influenza	0.19
L40	Psoriasis	0.19
E66	Obesity	0.18
M45	Ankylosing spondylitis	0.11

Code	Disease (pharma ICDs, n/a's deleted). Cancer in blue.	Net production £ per QALY
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
displ	***(average displaced QALY)***	£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
zero	*(zero BoI, WSB condition)*	£0
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

Source: G Roberts, Department of Health

Attributes of investment and expected disinvestment

- 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 (£13,322) per QALY
  - 23,000 eligible patients each year
- Attributes of benefit

Deaths	LYs	QALYs
0	0	3,225 (6,052)

WSB of £26,432 (or 0.441 QALYs) per QALY gained (ICD E11)

- Approval will cost the NHS £80m p.a.
- Attributes of benefit displaced each year

Deaths	LYs	QALYs
411	1,864	6,184

WSB of £11,611 (or 0.194 QALYs) per QALY displaced

What type of data and research could improve the estimate?

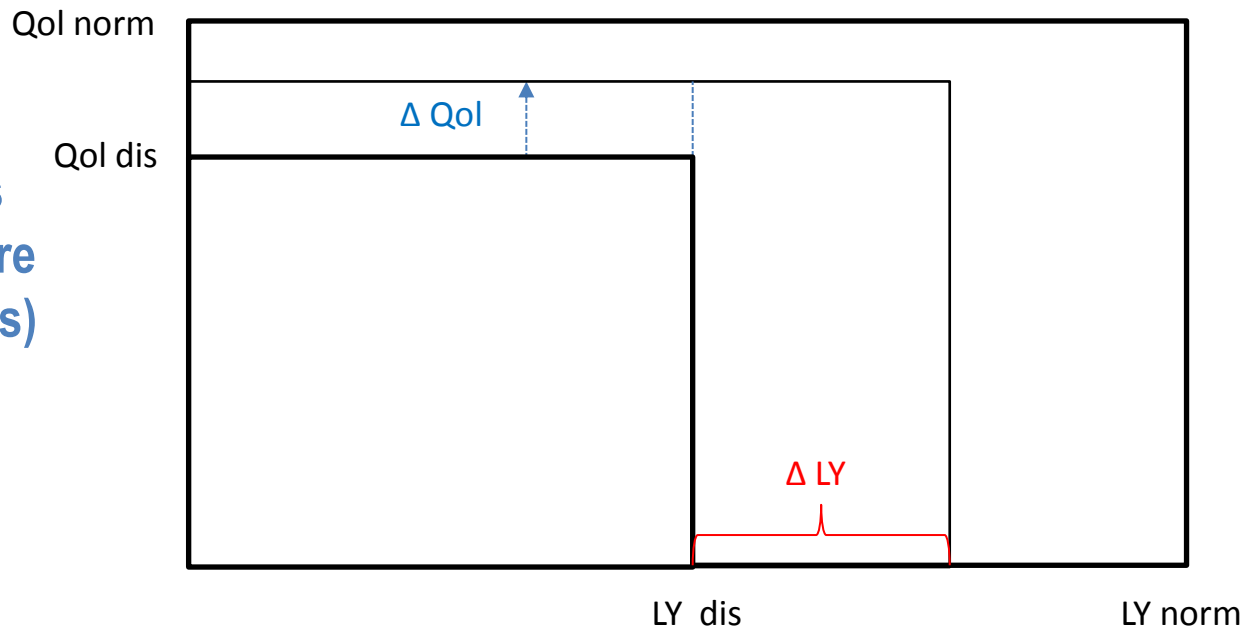
- Longer and more complex lag structure
  - Duration of effect on mortality might be feasible (capture more health effects)
  - Estimating life year effect of mortality more problematic
- Simultaneous estimation across PBCs
  - Likely to capture more health effects
- Evolving PBC data (PCT and CCG boundaries)
- Extending measures of health outcome
  - Analysis of PROMs data
  - IAPT and mental health outcomes
- Incidence (age and gender) and duration of disease
  - WHO GBD
  - GPRD

Additional slides

- Reserve slides if needed during discussion

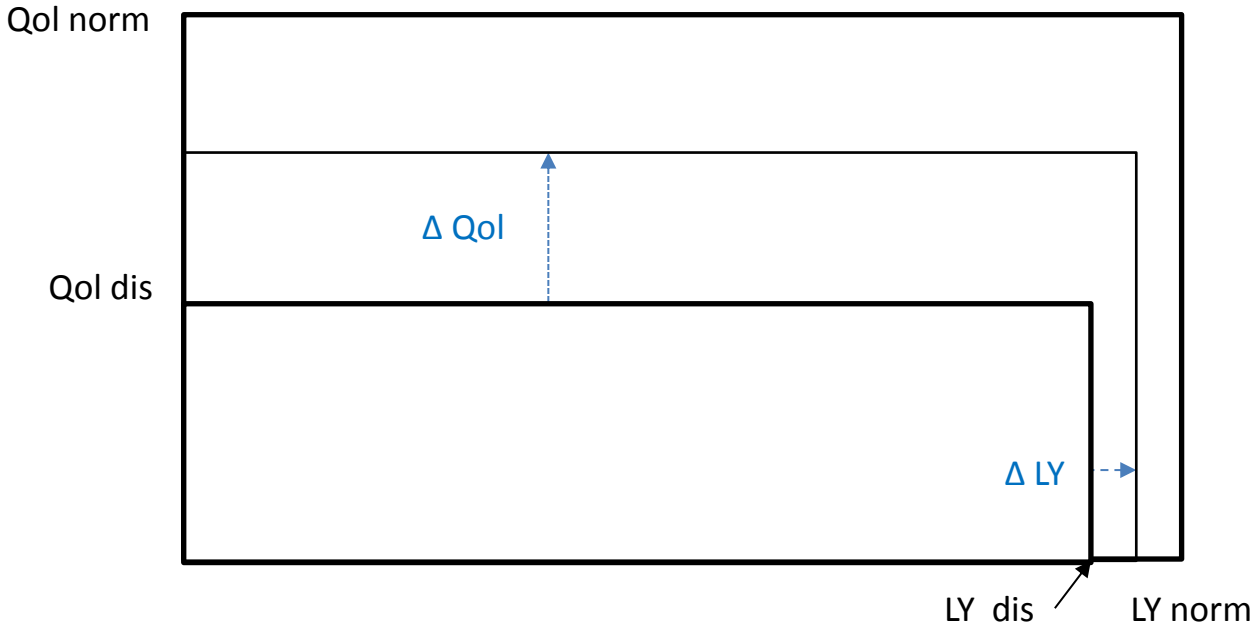
Surrogacy

Quality of life effects (each of 11PBCs where can estimate LY effects) % reduction in LY burden



Extrapolation

QALY effects (other 11PBCs) Same % effect on burden



Estimating production and consumption effects

Mechanism estimates prod / cons <u>without the treatment</u>..

Source: G Roberts, Department of Health

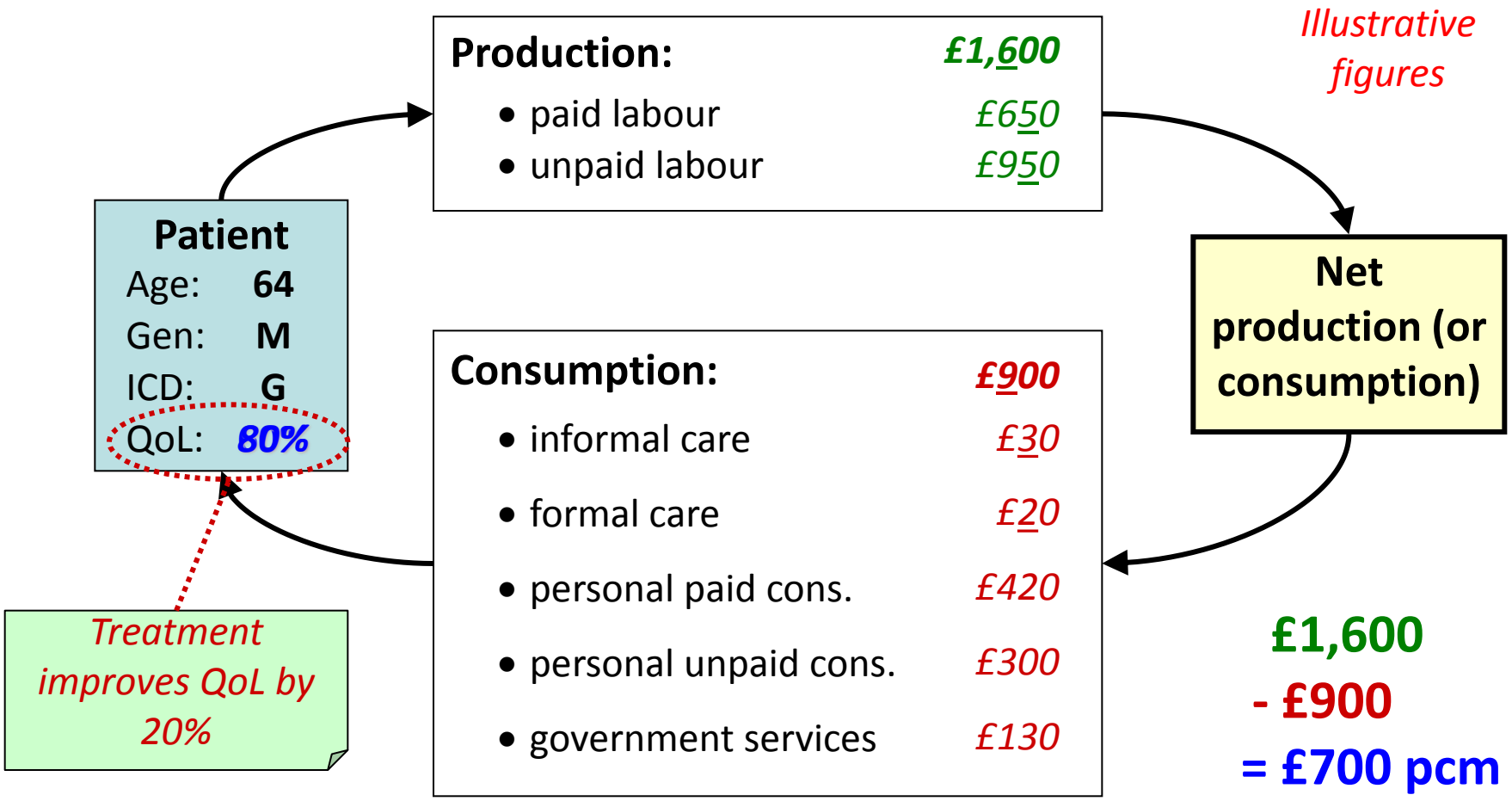
Estimating production and consumption effects

..which is compared to prod / cons with treatment to give impact

Source: G Roberts, Department of Health

Estimating production and consumption effects

..which is compared to prod / cons with treatment to give impact



Raising this patient's QoL from 60% to 80% generates £200pcm in net prod / cons

Source: G Roberts, Department of Health

Estimating production and consumption effects
Main data sources

Element	Dependent variables	Main data sources
Paid labour	**AGQ**	Annual Survey of Hours and Earnings (AG) Understanding Society (AQ)
Unpaid labour	**AGQ**	Time Use Survey (AG) Sick rate, derived from Understanding Soc. (Q)
Informal care	**AGIQ**	HoDAR
Formal care	**A(I)Q**	Adult Soc. Care Survey, GP Patient Survey, PSSRU data
Personal paid consumption	**A**	Living Costs and Food Survey
Personal unpaid consumption	**(const)**	Time Use Survey
Government services	**A**	Public Expenditure Statistical Analysis

Source: G Roberts, Department of Health

A methodology for measuring the Production and Consumption effects of health treatments

1. Policy context

2. Defining the production and consumption effects of treatments

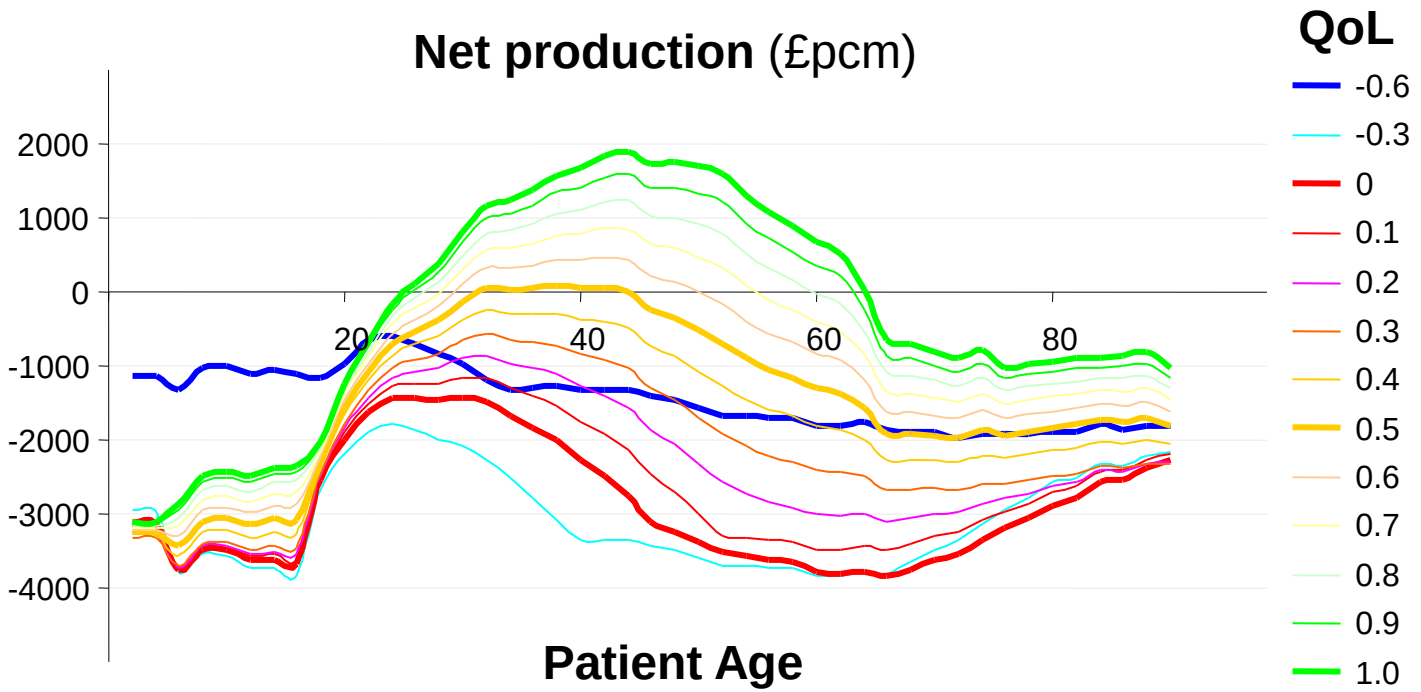
3. Estimating production and consumption effects

4. Results

Source: G Roberts, Department of Health

Results

Net production (or consumption) as a function of age and QoL



NB this is the rate of net production in a given state – not the treatment impact

Source: G Roberts, Department of Health

Production and consumption effects of health treatments

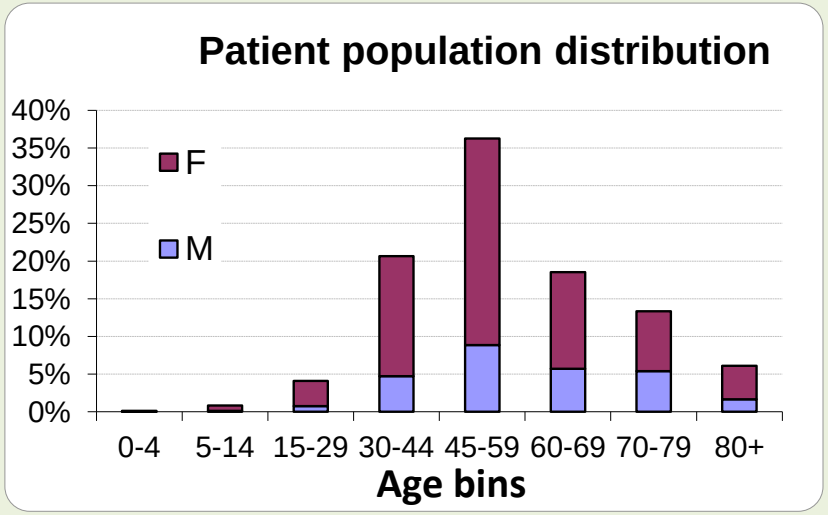
Estimation for ICD populations with a reference dataset

ICD

-eg M06: *Rheumatoid Arthritis*

Reference Dataset (1284 ICDs)

For each ICD: *distrib. of patients* (16 AG bins)



For <u>each AG bin</u> we know:

- Starting QoL (given current treatment)
- % of QALY gains in Length of Life (vs QoL)

> Can calculate net prod. for bin, and ICD

£net production per QALY gained in ICD

= **£30,034** / QALY gained

= **0.50 QALYs *worth*** / QALY gained

(*using DH social value of £60k / QALY*)

Source: G Roberts, Department of Health

Production and consumption effects of health treatments

Estimates across select ICDs in reference dataset

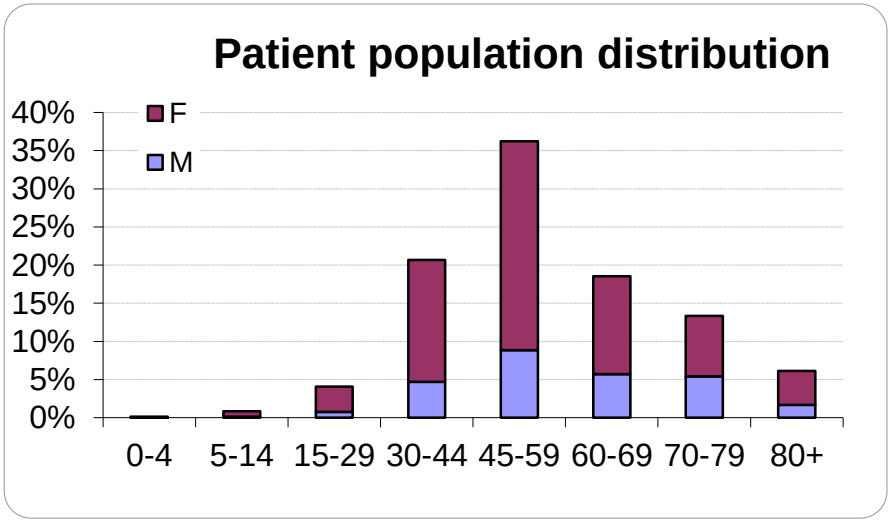
ICD Code	Disease	£net prod per QALY	QALYs' worth*	Net prod. vs displaced
M05	Rheumatoid arthritis	30,034	0.50	
E11	Diabetes	27,421	0.46	
F30	Depression	23,489	0.39	
F20	Schizophrenia	22,697	0.38	
G43	Migraine	20,604	0.34	
J45	Asthma	20,100	0.33	
K02	Dental caries	20,004	0.33	
K25	Gastric ulcer	19,697	0.33	
M81	Osteoporosis	17,910	0.30	
G35	Multiple sclerosis	15,482	0.26	
G40	Epilepsy	14,245	0.24	
J03	Acute tonsillitis	13,011	0.22	
displ	***(average displaced QALY)***	11,611	0.19	
E66	Obesity	8,138	0.14	
C53	Cervical cancer	6,912	0.12	
G30	Alzheimer's disease	351	0.01	
I64	Stroke	-6,949	-0.12	
C18	Colon cancer	-8,061	-0.13	
C61	Prostate cancer	-10,602	-0.18	
I21	Acute myocardial infarction	-14,395	-0.24	
J10	Influenza	-21,568	-0.36	
C34	Lung cancer	-36,067	-0.60	
C25	Pancreatic cancer	-53,860	-0.90	

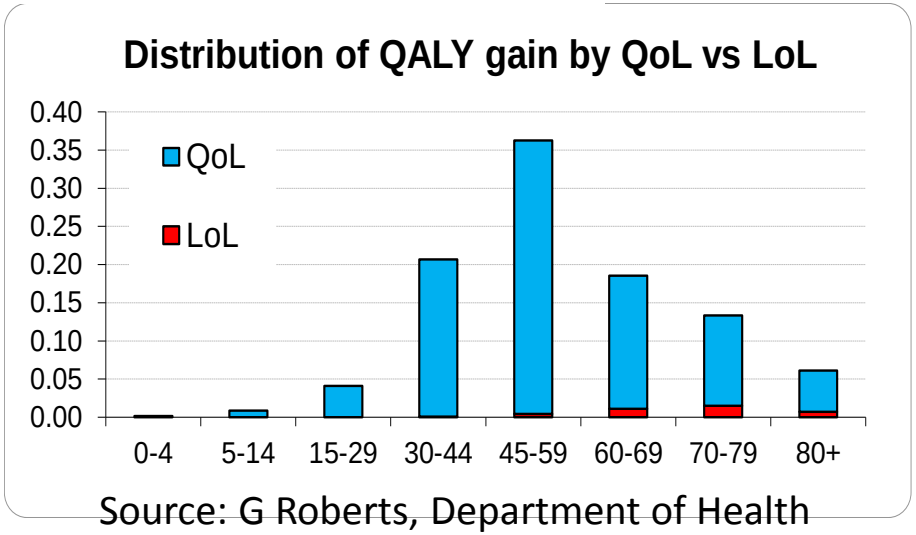
Source: G Roberts, Department of Health

Production and consumption effects of health treatments

M05 Rheumatoid arthritis: *results by category, and key inputs*

Category	£ / QALY of gain
total production impact	**24,529**
Paid production	10,098
Unpaid production	14,431
total consumption impact	**-5,505**
Formal care consumption	-1,753
Informal care consumption	-8,012
Private paid consumption	1,490
Private unpaid consumption	1,653
Government consumption	1,116
TOTAL WSBs	**30,034**





Source: G Roberts, Department of Health

Code	Disease (pharma ICDs). Cancer in blue.	Burden of Illness Absolute QALY loss
C22	Liver cancer	10.70
C25	Pancreatic cancer	9.97
C34	Lung cancer	9.68
F20	Schizophrenia	7.62
G35	Multiple sclerosis	6.18
C92	Myeloid leukaemia	6.15
G20	Parkinson's disease	4.60
C90	Myeloma	4.45
J43	Emphysema and COPD	3.80
C64	Kidney cancer	3.75
F30	Depression	3.63
M05	Rheumatoid arthritis	2.83
E11	Diabetes	2.68
displ	***(average displaced QALY)***	2.07
J45	Asthma	1.86
G30	Alzheimer's disease	1.68
F03	Dementia	1.68
G40	Epilepsy	1.32
C18	Colon cancer	1.28
I26	Embolisms, fibrillation, thrombosis	1.16
C61	Prostate cancer	1.06
I21	Acute myocardial infarction	1.00
I64	Stroke	0.83
C53	Cervical cancer	0.60
C50	Breast cancer	0.55
A40	Streptococcal septicaemia	0.38
J30	Allergic rhinitis	0.30
M81	Osteoporosis	0.28
K50	Irritable Bowel Syndrome	0.26
J10	Influenza	0.19
L40	Psoriasis	0.19
E66	Obesity	0.18
M45	Ankylosing spondylitis	0.11

Source: G Roberts, Department of Health

Code	Disease (pharma ICDs). Cancer in blue.	Burden of Illness - proportional (QALY loss / Expected QALYs if healthy) Expected QALYs if healthy	Prop shortfall
C22	Liver cancer	14	73%
C25	Pancreatic cancer	13	73%
C34	Lung cancer	14	71%
C92	Myeloid leukaemia	21	38%
G20	Parkinson's disease	17	31%
C90	Myeloma	19	31%
C64	Kidney cancer	28	22%
G35	Multiple sclerosis	46	18%
J43	Emphysema and COPD	26	17%
G30	Alzheimer's disease	11	14%
F03	Dementia	11	14%
F20	Schizophrenia	63	12%
M05	Rheumatoid arthritis	28	11%
C61	Prostate cancer	18	11%
I26	Embolisms, fibrillation, thrombosis	22	11%
E11	Diabetes	27	11%
C18	Colon cancer	23	10%
I21	Acute myocardial infarction	19	9%
I64	Stroke	24	8%
displ	***(average displaced QALY)***	42	8%
F30	Depression	58	6%
G40	Epilepsy	44	4%
J45	Asthma	61	4%
C50	Breast cancer	33	3%
C53	Cervical cancer	39	3%
L40	Psoriasis	13	2%
J10	Influenza	38	2%
M81	Osteoporosis	25	2%
J30	Allergic rhinitis	45	2%
A40	Streptococcal septicaemia	59	2%
K50	Irritable Bowel Syndrome	46	1%
E66	Obesity	66	0%
M45	Ankylosing spondylitis	30	0%

Source: G Roberts, Department of Health

Code	Disease (pharma ICDs, n/a's deleted). Cancer in blue.	Net production £ per QALY
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
displ	***(average displaced QALY)***	£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
zero	*(zero BoI, WSB condition)*	£0
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

Source: G Roberts, Department of Health