Session III
Value of information analysis

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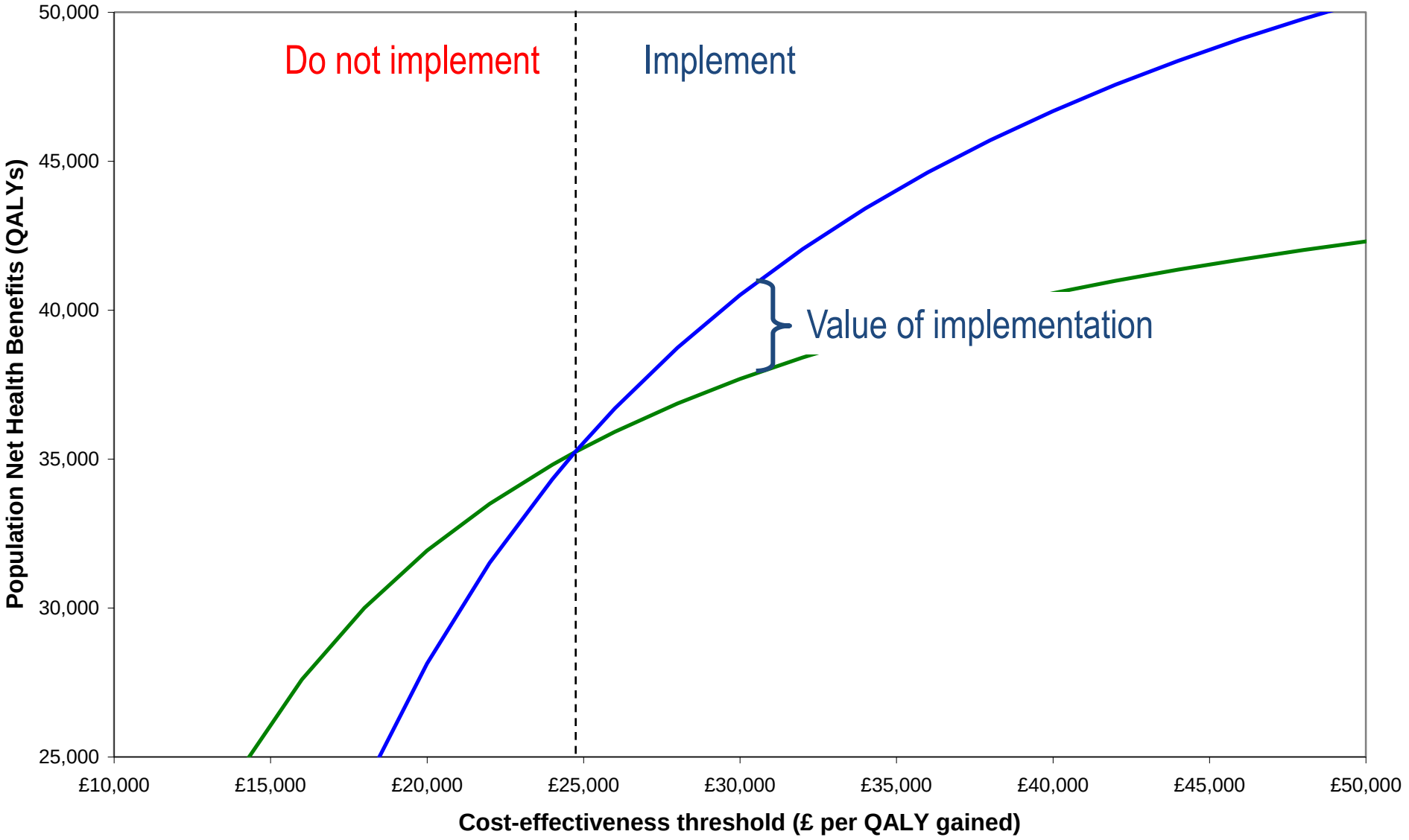
Distinguish principles from methods

- What assessments need to be made?
  - Either implicit or judgement informed by explicit analysis
- Which methods might be useful?
  - No analysis can ever capture all aspects of value
  - Does it directly address the assessments required?
  - Is it feasible within existing constraints?
  - Does it capture enough to be a useful starting point?
- Will we make better decisions?
  - Never know the counterfactual for sure
  - Decisions are better if more accountable to:
    - Reason
    - Evidence and the scientific value judgments required
    - Social value judgment that are unavoidable
  - Enable informed scrutiny by those with a legitimate interest

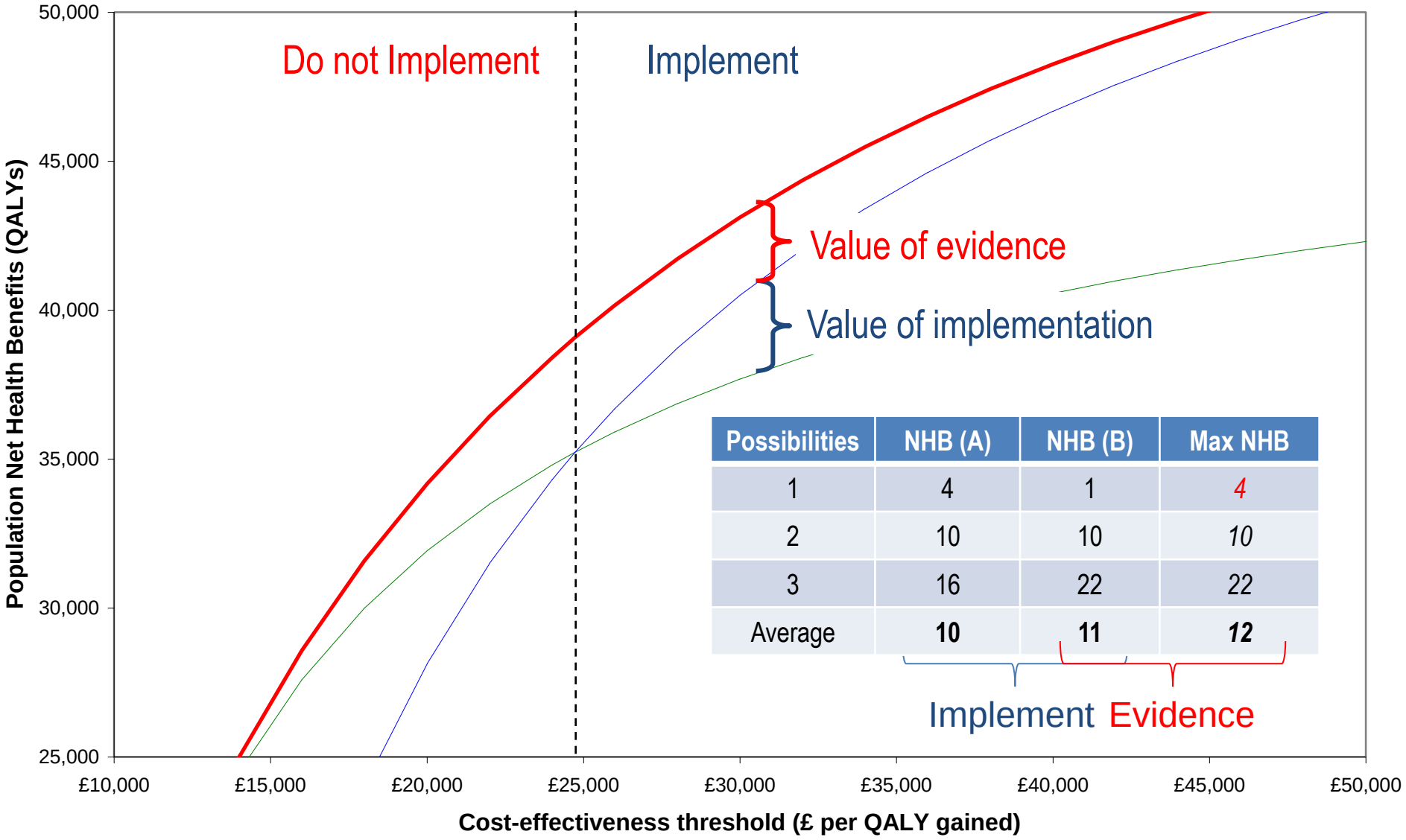
Principles of VoI have nothing to do with any of them!

- NHS is collectively funded and budget constrained
  - Primary purpose is to improve health (of all)
- NHS costs and the threshold
  - NHS costs matter – they are other (unknown) patients health
  - How much health likely to be forgone – the NICE threshold
- EQ-5D QALYs?
  - Health gained and forgone in very different areas
  - Need a metric of health that is comparable
  - Reflects important dimensions (length and its quality
  - Weights based on choices (preferences)
  - From those for whom decisions are being made on their behalf

Implement the new technology?



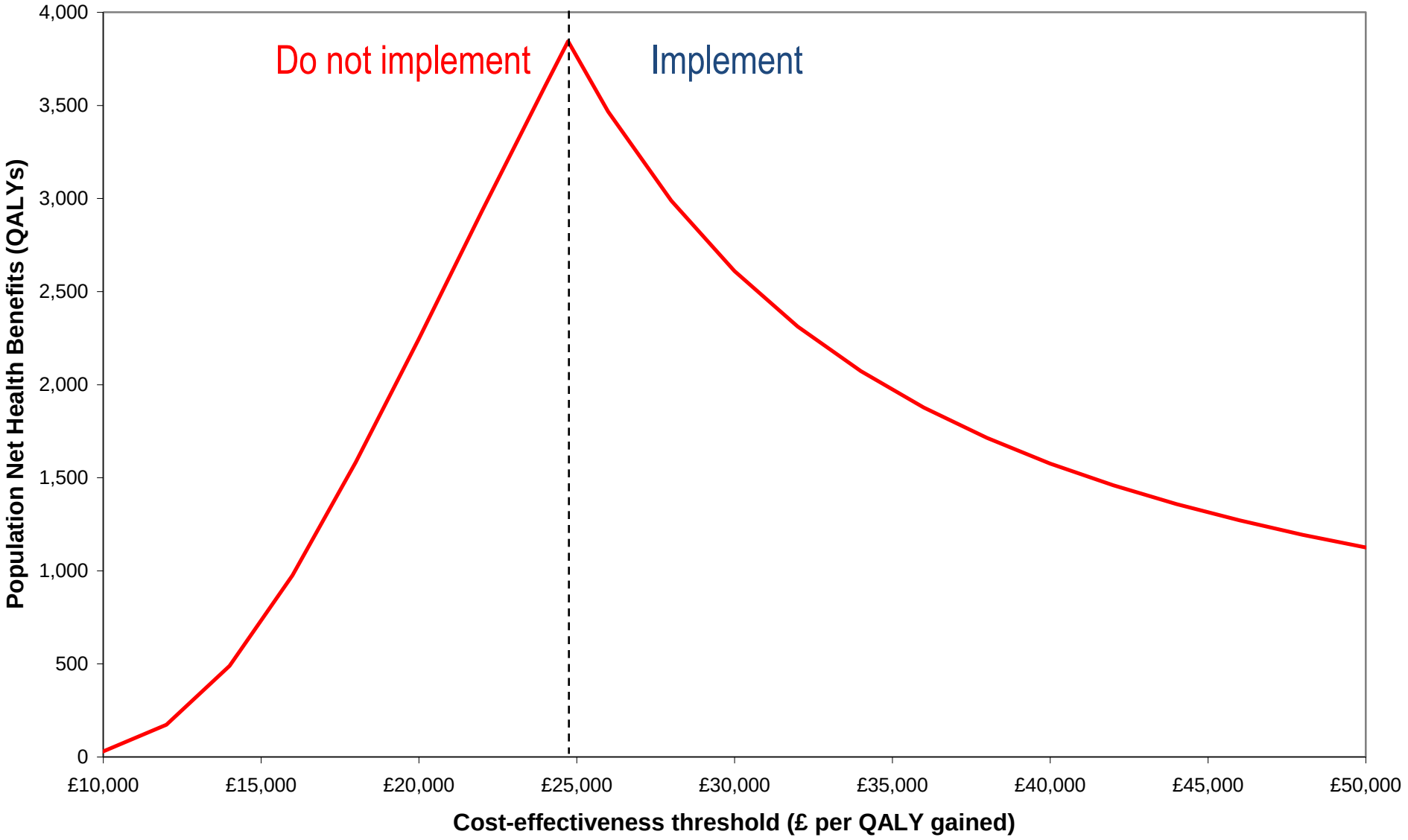
Value of additional evidence



Possibilities	NHB (A)	NHB (B)	Max NHB
1	4	1	*4*
2	10	10	*10*
3	16	22	*22*
Average	**10**	**11**	***12***

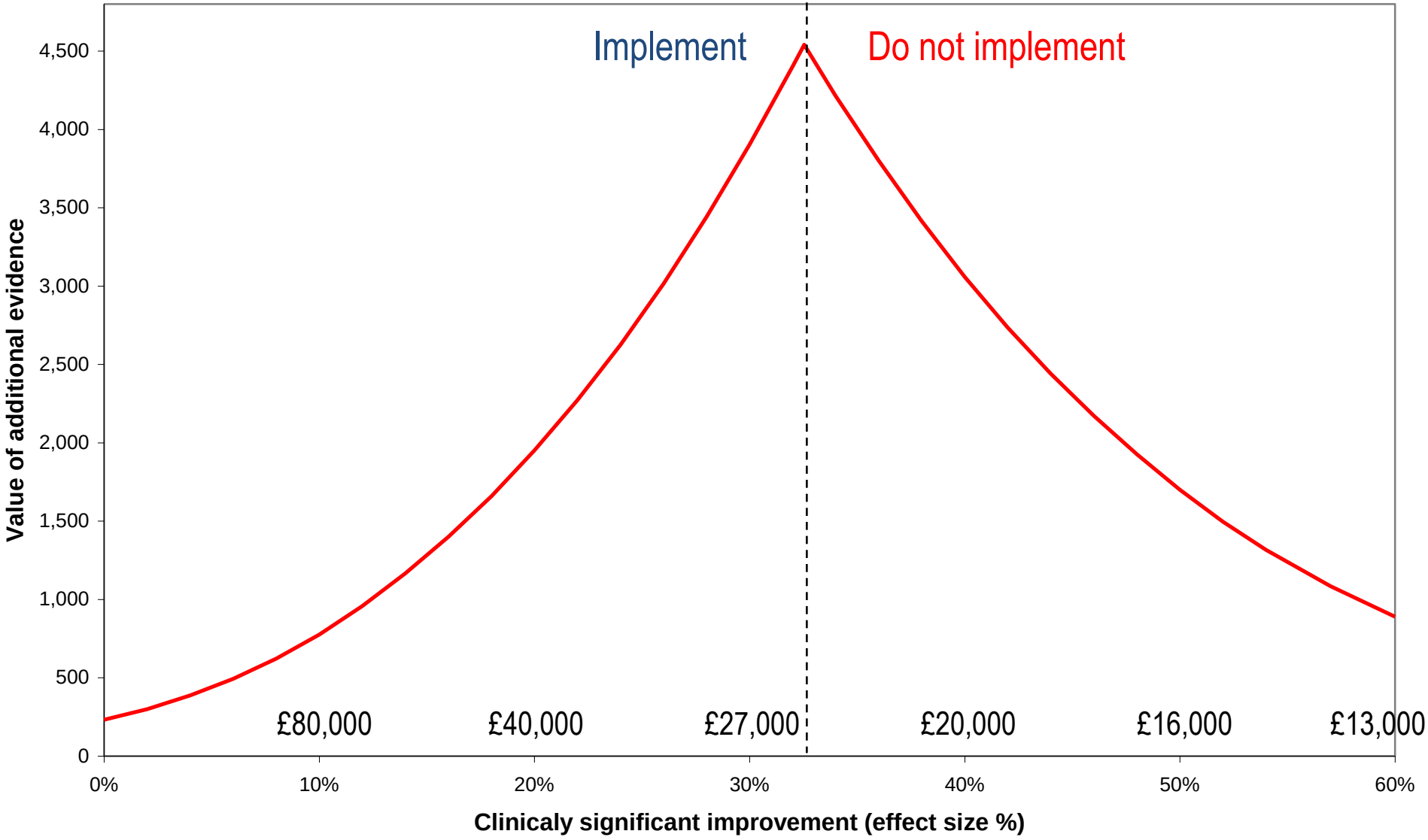
Implement Evidence

Value of additional evidence



What is clinically significant?

(effect size sufficient to change practice)



Keeping it simple (and real)

A re-analysis of the CRASH trial for Iain Chalmers and Ian Roberts

(very large international multi centre trial of steroids in TBI, 2004)

- VoI based on what was available in the CfS
  - Based only on std meta analysis of mortality endpoint
  - OR applied to UK population, baseline and implementation (12% steroids)
  - 634 lives pa (steroids,12%) and 298 lives pa (no steroids, 88%)
- Considering impact on disability
  - An 'effectiveness' model
  - Decompose survival effect into GOS, link to LE and to EQ-5D (GOS states)
  - 10,620 LY full health (steroids,12%) and 6,292 LY full health (no steroids, 88%)
- Adding in resource use
  - Same model - makes little difference to the decisions
  - 760 QALYs pa or equivalent to £15.2m in NHS resources
- Was CRASH too big (stopped early at n=10,060)?
  - EVSI suggested lower sample size (report earlier and save more lives)
  - Larger sample size if implementation is function of $p<0.01$

Early experiences in the UK

Pilot studies for NCCHTA (2003) and NICE (2004)

- Is further research required
  - Research is not needed
  - Research is a priority
- What type of research
  - RCTs of treatment effect
  - Quality of life, natural history and resource use
- Which subgroups
  - All subgroups should be included in research
  - Only worthwhile for certain groups
- Which comparators
  - Head to head comparisons are needed
  - Some comparators could be ruled out
- Which endpoints
- Length of follow-up

A cool but unfamiliar solution for decision makers who didn't think they had a problem!

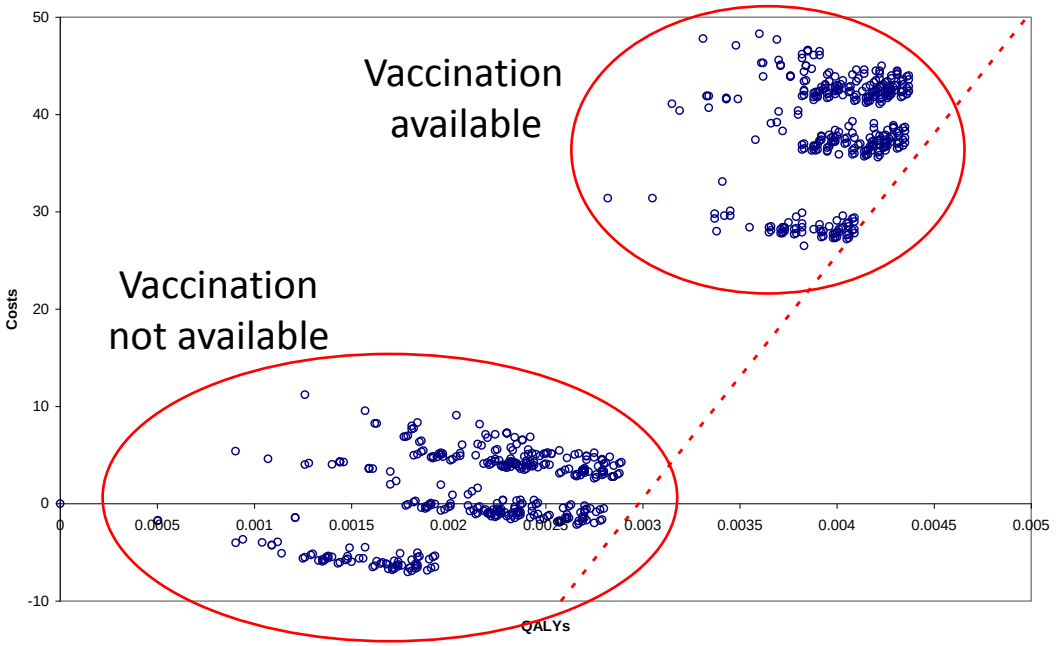
Current policy impact

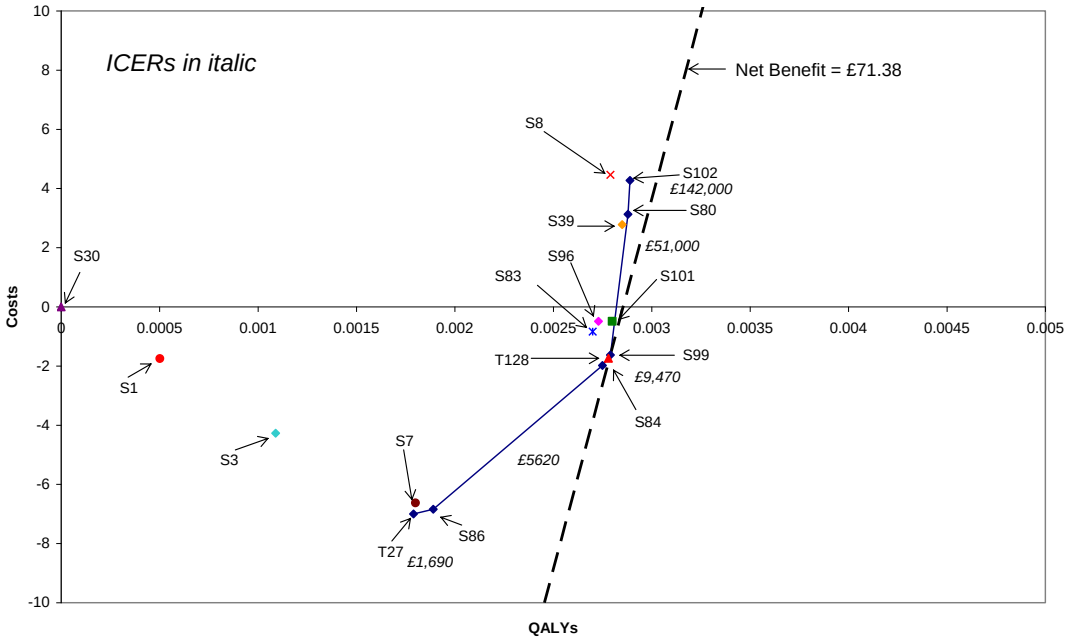
- Difficult/important decisions - NCCTHA (NIHR)
  - Group B Streptococcal in neonates
  - Duration of treatment with clopidogrel
- Iterative process – MRC (NIHR)
  - Vacuum assisted closure (see Sores et al 2011, 2012)
  - MRC wounds programme (underway)
- NICE
  - No remit for research (can only make recommendations)
  - PSA required but VoI recommended (2004 and 2008)
  - Pressure to stream line and speed the process (STA)
  - Limited impact of recommendations on research commissioning
  - Research decisions without regard for needs of NICE/NHS decisions
  - Approval/recommendations without regard for research needs
- Only in research report (MRC/NIHR) (Claxton et al 2011 and 2012)
  - NICE TA methods review 2012, also MTAC, Diagnostics and Public Health
- Value Based Pricing 2014 (Department of Health)
  - Qualitative assessment identify candidates for quantitative analysis
  - Type of evidence and research, irrecoverable costs

Research priorities

- GBS (Colbourn et al 2007)
  - Inform trial commissioning
  - Largest trial in the UK
  - Large % of HTA budget

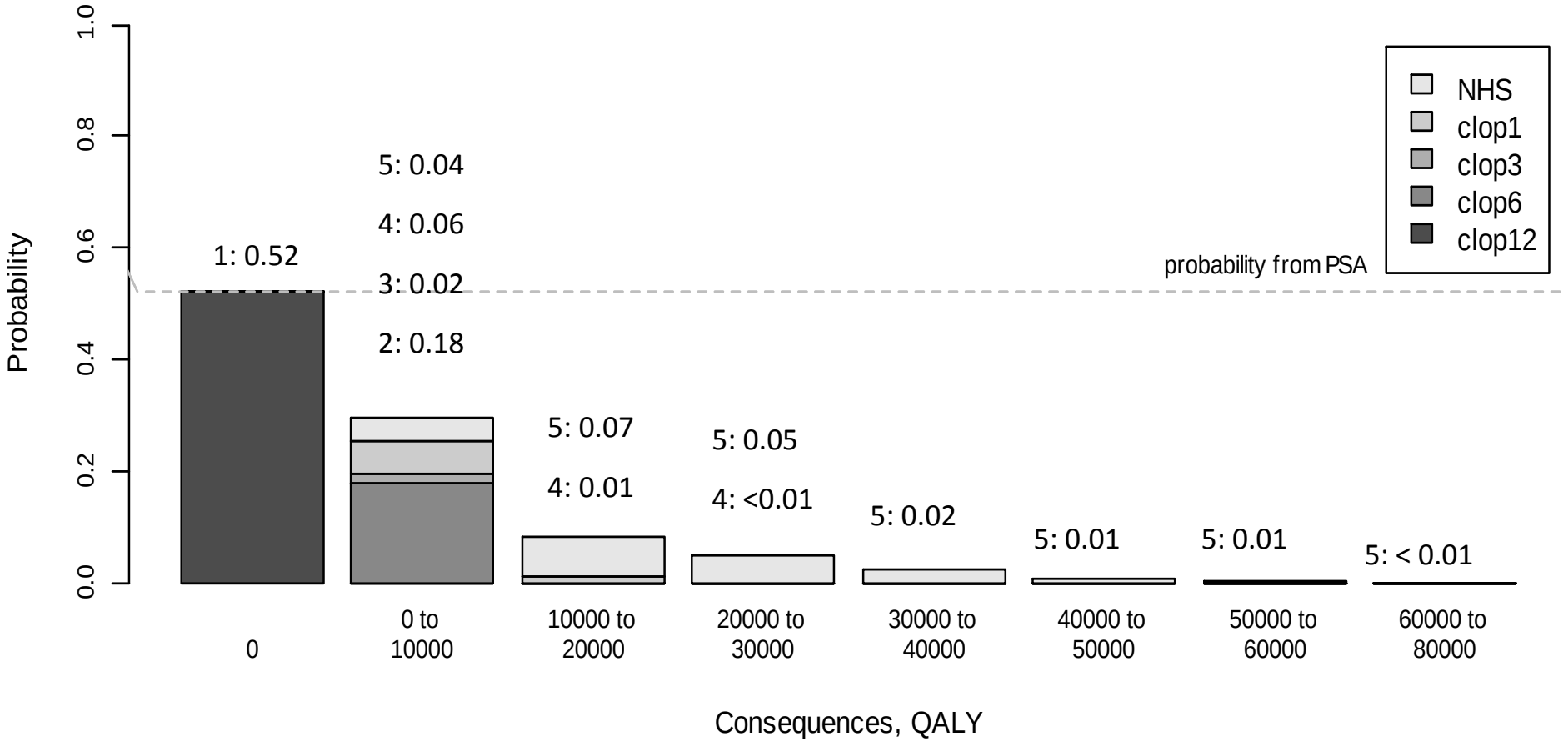
Risk Groups	EVPI	Error probability
Preterm:		
1. Planned LSCS	5,281,333	0.413
2. Previous GBS baby	7,820	0.141
3. GBS positive swab	81,600	0.027
4. Pyrexia	539,467	0.22
5. Prelabour ROM	12,806,667	0.42
6. Intact membranes	4,193,333	0.141
Term:		
7. Planned LSCS	1,586,667	0.328
8. Previous GBS baby	30,600	0.394
9. GBS positive swab	68,000	0.027
10. Pyrexia	581,400	0.283
11. Prolonged ROM	4,533,333	0.424
12. No risk factors	2,040,000	0.161
Total EVPI	31,750,220	





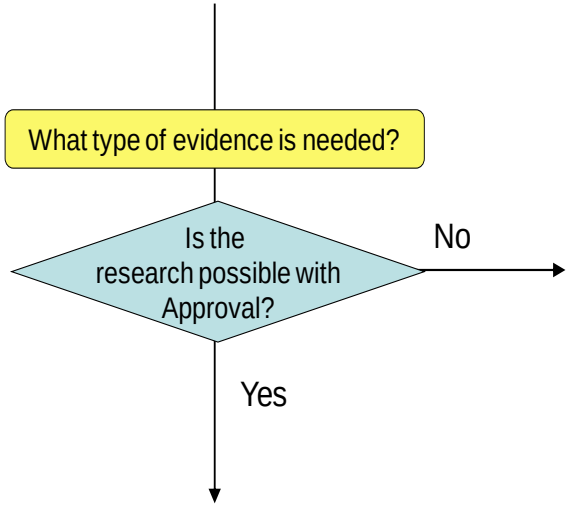
What could be potentially gained from research

Figure 3.4b Distribution of the consequences of uncertainty for CLOP



What type of research is needed?

- Type of evidence needed?
  i. Importance of parameters (values that change the decision)
  ii. Uncertainty in possible values (how likely to change)
  iii. What might be gained (expected consequences)
- What type of research is required to generate it?
- Can be it conducted once approved for widespread NHS use?



i) Importance: what values change decisions (CLOP)

	Parameter		Mean value	Clop12	Clop6	Clop3	Clop1	NHS
Natural history	1	P_die_0.1	0.032	0 to 0.10	0.11 to 0.54	0.54 to 0.63	0.63 to 1	-
	2	P_NFMI_0.1	0.040	0 to 0.14	0.14 to 0.71	0.71 to 0.82	0.82 to 1	-
	3	P_die_1.3	0.022	0 to 0.10	0.10 to 0.55	0.55 to 1	-	-
	4	P_NFMI_1.3	0.004	0 to 0.10	0.10 to 0.7	0.7 to 1	-	-
	5	P_die_3.6	0.023	0.01 to 0.10	0.10 to 1	0 to 0.01	-	-
	6	P_NFMI_3.6	0.011	0 to 0.11	0.11 to 1	-	-	-
	7	P_die_6.12	0.024	0.02 to 1	0 to 0.02	-	-	-
	8	P_NFMI_6.12	0.009	0.005 to 1	0 to 0.005	-	-	-
	9	TP_AC	0.018	0 to 0.06	0.06 to 1	-	-	-
	10	TP_AD	0.072	0 to 0.08	0.08 to 0.10	-	-	0.10 to 1
	11	TP_CD	0.188	0.12 to 1	0 to 0.12	-	-	-
	12	TP_BD	0.070	0.06 to 1	0.04 to 0.06	-	-	0 to 0.04
Utilities	13	U_Well	0.798	0.29 to 1	0 to 0.29	-	-	-
	14	U_Well1	0.930	0.90 to 1	0.74 to 0.90	-	-	0 to 0.74
	15	U_NFMI	0.801	0 to 1	-	-	-	-
	16	U_POSTMI	0.931	0 to 1	-	-	-	-
RE	17	RR_death	0.931	0 to 0.93	0.94 to 0.97	0.97 to 0.98	0.98 to 0.99	1.00 to max*
	18	RR_NFMI	0.710	0 to 0.82	0.83 to 1.55	1.56 to 1.83	-	1.84 to max*
Costs	19	C_Well	2061.5	0 to 2690	2690 to 5611	-	-	5611 to max*
	20	C_MI_LT	6050.0	0 to max*	-	-	-	-
	21	C_PostMI	2309.7	870 to max*	0 to 870	-	-	-
	22	TC_Well_Dead	871.5	0 to 20474	20474 to max*	-	-	-
	23	C_t1	895.1	0 to 910	910 to max*	-	-	-
	24	C_t2	651.6	630 to max*	0 to 630	-	-	-
	25	C_t3	524.2	370 to max*	-	0 to 370	-	-
	26	C_t4	434.8	150 to max*	-	-	0 to 150	-
	27	C_t5	329.8	0 to max	-	-	-	-

ii) How likely to change decisions (CLOP)

Table 3.6a Probabilities associated with parameter values (CLOP)

	Parameter	Clop12	Clop6	Clop3	Clop1	NHS
Natural history	1 P_die_0.1	1	-	-	-	-
	2 P_NFMI_0.1	1	-	-	-	-
	3 P_die_1.3	1	-	-	-	-
	4 P_NFMI_1.3	1	-	-	-	-
	5 P_die_3.6	1	-	-	-	-
	6 P_NFMI_3.6	1	-	-	-	-
	7 P_die_6.12	0.65	0.35	-	-	-
	8 P_NFMI_6.12	0.91	0.09	-	-	-
	9 TP_AC	1	-	-	-	-
	10 TP_AD	0.83	0.17	-	-	-
	11 TP_CD	1	-	-	-	-
	12 TP_BD	0.85	0.15	-	-	-
Utilities	13 U_Well	1	-	-	-	-
	14 U_Well1	0.94	0.06	-	-	-
	15 U_NFMI	1	-	-	-	-
	16 U_POSTMI	1	-	-	-	-
RE	17 RR_death	0.55	0.18	0.01	0.10	0.16
	18 RR_NFMI	0.97	0.03	-	-	-
Costs	19 C_Well	0.78	0.19	-	-	0.03
	20 C_MI_LT	1	-	-	-	-
	21 C_PostMI	0.89	0.11	-	-	-
	22 TC_Well_Dead	1	-	-	-	-
	23 C_t1	0.95	0.05	-	-	-
	24 C_t2	0.99	0.01	-	-	-
	25 C_t3	1	-	-	-	-
	26 C_t4	1	-	-	-	-
	27 C_t5	1	-	-	-	-

iii) Expected consequences (importance and uncertainty)

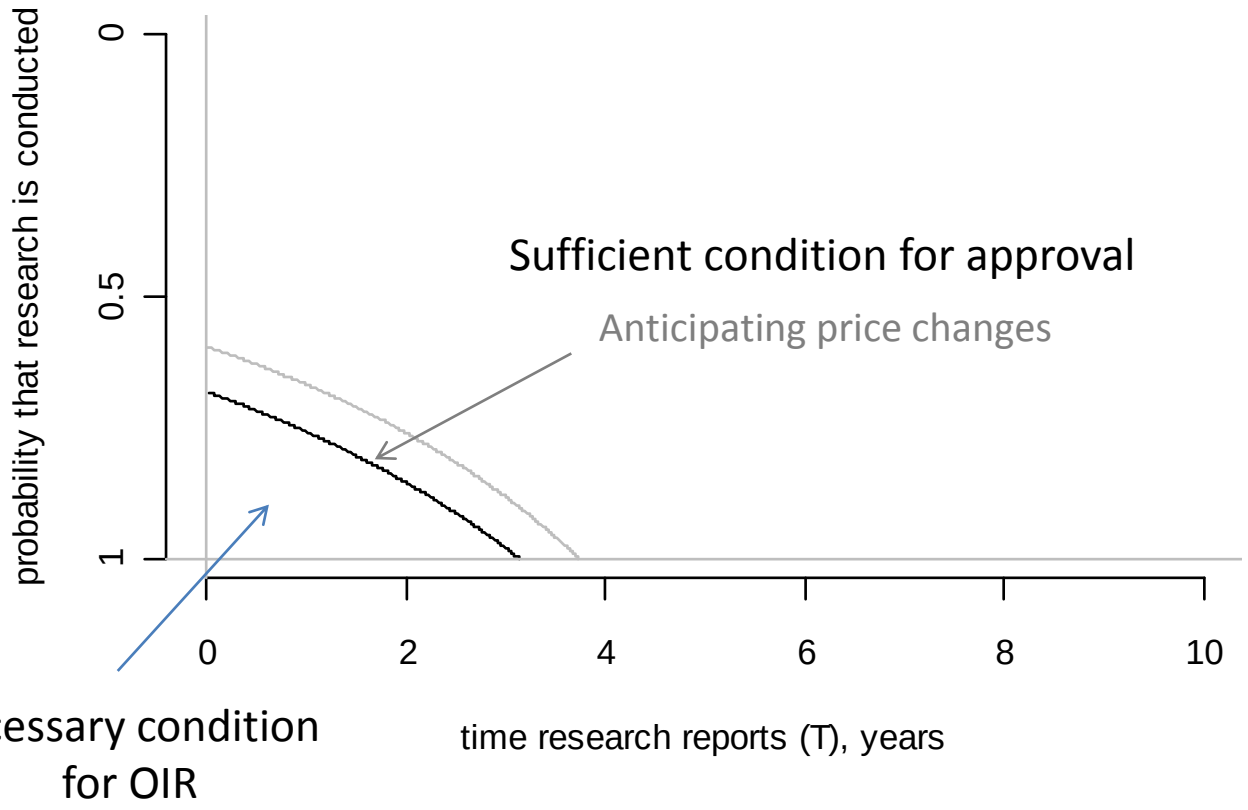
Table 3.6b Consequences of uncertainty associated with parameter values (CLOP)

		Decomposed by treatment choice					
Parameter		clop12	clop6	clop3	clop1	NHS	Overall
Natural history*	1 P_die_0.1	0	-	-	-	-	-
	2 P_NFMI_0.1	0	-	-	-	-	-
	3 P_die_1.3	0	-	-	-	-	-
	4 P_NFMI_1.3	0	-	-	-	-	-
	5 P_die_3.6	0	-	-	-	-	-
	6 P_NFMI_3.6	0	-	-	-	-	-
	7 P_die_6.12	0	250	-	-	-	250
	8 P_NFMI_6.12	0	9	-	-	-	9
	9 TP_AC	0	-	-	-	-	-
	10 TP_AD	0	47	-	-	-	47
	11 TP_CD	0	-	-	-	-	-
	12 TP_BD	0	35	-	-	-	35
Utilities*	13 U_Well	0	-	-	-	-	-
	14 U_Well1	0	10	-	-	-	10
	15 U_NFMI	0	-	-	-	-	-
	16 U_POSTMI	0	-	-	-	-	-
RE	17 RR_death	0	284	16	518	3614	4433
	18 RR_NFMI	0	3	-	-	-	3
Costs*	19 C_Well	0	153	-	-	321	474
	20 C_MI_LT	0	-	-	-	-	-
	21 C_PostMI	0	8	-	-	-	8
	22 TC_Well_Dead	0	-	-	-	-	-
	23 C_t1	0	8	-	-	-	8
	24 C_t2	0	0	-	-	-	-
	25 C_t3	0	-	-	-	-	-
	26 C_t4	0	-	-	-	-	-
	27 C_t5	0	-	-	-	-	-

Implementation and research decisions

Implement but forego evidence? (Griffin et al, 2011, Claxton et al 2012)

- Trade net benefits for current and future populations
- Depends on time research will take and how likely to report
- Generic entry reduces the future value of the information



Heterogeneity, subgroups and individualised care

RCT evidence on NHB of new technology B

Patient ID	A	B
i	2	?
ii	4	?
iii	?	1
iv	?	3
Average	**3**	**2**

Averages are uncertain so might be value in a larger sample

What does joint distribution look like?

Potential value

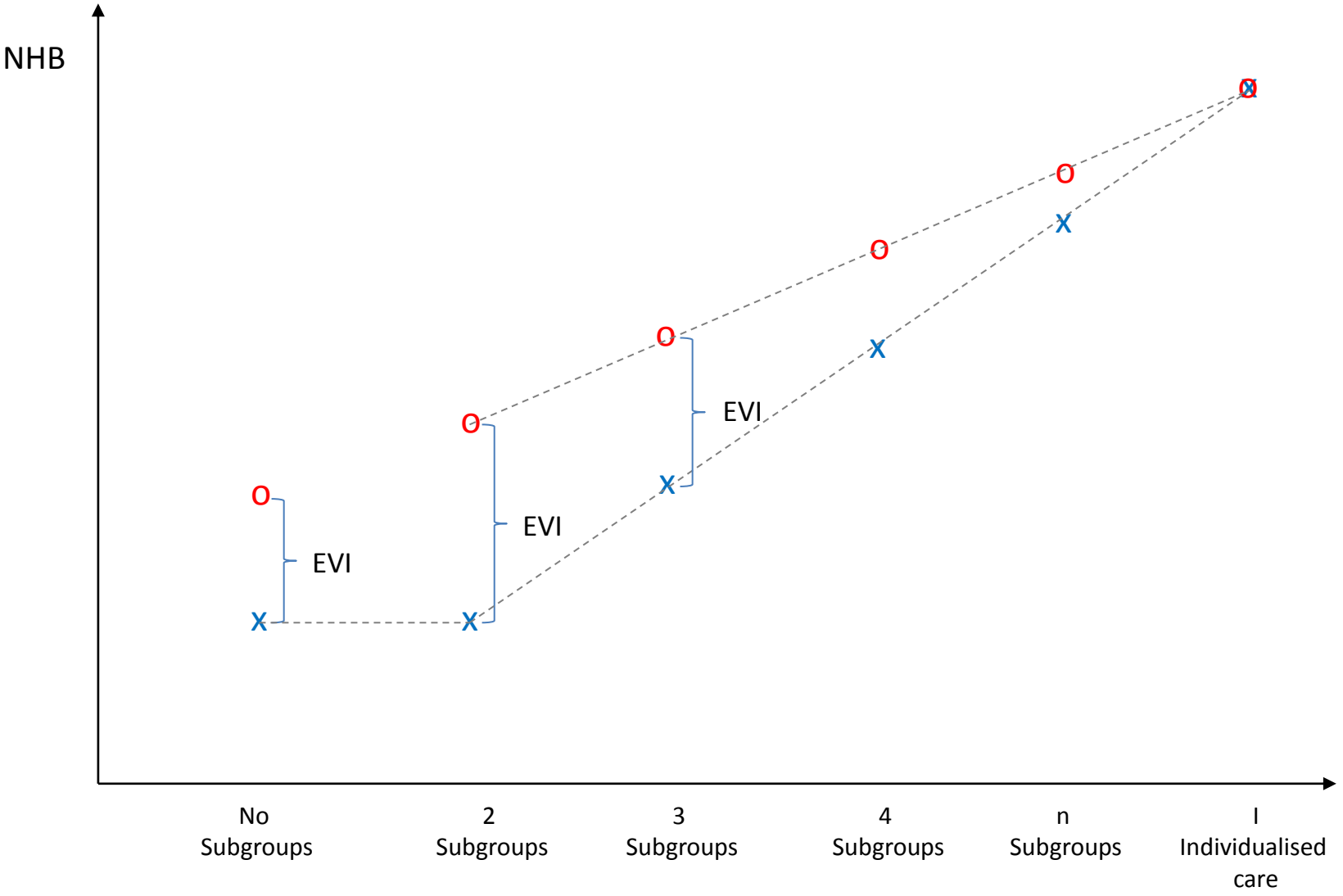
Patient ID	A	B	Choice	Gain
i	2	1	A	-
ii	4	3	A	-
iii	2	1	A	-
iv	4	3	A	-
Average	3	2		

0

Patient ID	A	B	Choice	Gain
i	2	3	B	1
ii	4	1	A	-
iii	4	1	A	-
iv	2	3	B	1
Average	3	2		

2

Uncertainty, subgroups and individualised care



Policy choices (individual choice, subgroups or restrict access)

- Invest resources in:
  - Implementing technologies with current evidence
  - Reduce uncertainty (additional evidence about average NHBs)
  - Make sources of variability observable (payers and/or individuals)
- Observing more sources of variability is costly
  - Costs of acquiring the information
    - Group membership and NHB given membership
  - Costly to communicate, implement complex findings/guidance
  - Individual choices may not be ‘efficient’
  - Additional uncertainty *is not* a cost
- Understand how individuals select
  - Estimate the joint distribution (observe selection)
  - Understand costs and benefits of individual choice
  - How selection might be influenced

Other things in the brief

- Costs of research
  - EVPI(£) > NHS R+D budget cost is not enough is its not the same pot
  - What are the other opportunities forgone (funding rounds to compare value)?
  - Generate more health than other federal expenditure regarded as good value?
    - Some caveats when budget constrained (see McKenna and Claxton, JHE 2010)
- Comparable metric or other PCOs
  - Weight different metrics (explicitly, consistently including deliberatively)
  - Allocate funds to different areas first
    - Arbitrary and implies a (hidden and not evidenced) weight anyway
- Population and time horizon (durability)
  - Relevant US patient population, central estimate of incidence, discount rate
  - Time horizon for the information is proxy for complex prospect (Philips 2008)
  - Consider important predictable events but use range of fixed horizons as a proxy

Final things in the brief

- Rarity?
  - NICE context
    - Lower EVI means willing to approve at a lower standard of evidence
    - Less likely to restrict access until uncertainty is resolved (OIR recommendation)
  - PCORIs problem?
    - If evidence found to be sufficient (no need to fund further research) other agents/ stakeholders have a duty to get it implemented
    - Justify and weight health gains more highly for rarity alone (in my view its not ethical)
- Implementation and EVI?
  - Without implementation value of research is not realised
  - Massive value of implementation without the need for research
  - Are scarce research resources the best or most efficient way to improve implementation?
- What is PCORIs job?
  - Commission research that really matters for the long run
  - Others have a duty to implement and fix things
  - Maybe if can help at limited opportunity costs for valuable evidence

Not in the brief and there wasn't time

- Structural uncertainty
  - Parameterisation (missing parameters from a meta model)
  - Statistical models, AIC, DIC and validity of instruments in selections models
  - Probabilistic scenarios
    - Value of resolving which scenarios is 'true'
  - Collect data that will challenge structural assumptions
- Computation
  - Linear approximations (Welton, Ades)
  - Emulators (Oakley) and (Strong)
  - Search algorithms (Conti and Claxton)
  - Iterative – keep it simple until it really matters (use stuff to hand resist descriptive realism)
- Elicitation
  - Increasing experience of practicalities and development of methods
  - Models/analysis are just a rather elaborate (but accountable) way of forming a prior
  - If you cant afford analysis – just pick your prior – you will (implicitly) anyway!