DANGEROUS OMISSIONS:

The consequences of ignoring decision uncertainty

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Introduction

When determining which technologies to reimburse within a health care system there are two conceptually distinct but simultaneous decisions:

1) Should a technology be adopted given the existing evidence (and the current uncertainty)?

2) Is additional evidence required to support the adoption decision?

Claxton K, The Irrelevance of Inference: a decision-making approach to the stochastic evaluation of health care technologies. J Health Econ 1999; 18: 342-364

Overview

- Decision theory
- The policy environment
- Decision rules incorporating the opportunity losses of adoption and rejection
- Incorporating uncertainty
- Discussion and Conclusions

Decision theory and value of information

Decision-making with uncertainty

- The decision to adopt a technology
  - Objective of health care system
    - Maximise health subject to budget constraint
  - Cost-effectiveness analysis
    - Compare health gained with new intervention to health displaced in transferring resources from existing programmes
- The decision to acquire more evidence
  - Value of information
    - Compare value of reducing expected cost of uncertainty to health displaced by allocating resources to research

The adoption decision

- Objective: maximise health gains from available resources
  - Simplifying conditions: absence of irreversibility and sunk costs (*Palmer and Smith 2002, Eckermann and Willan 2008)*

Decision to adopt technology, **j**, depends on

- expected cost, C_j
- expected outcomes, Q_j
- cost-effectiveness threshold, λ

Net benefit framework: $NB_j = Q_j - C_j/\lambda$

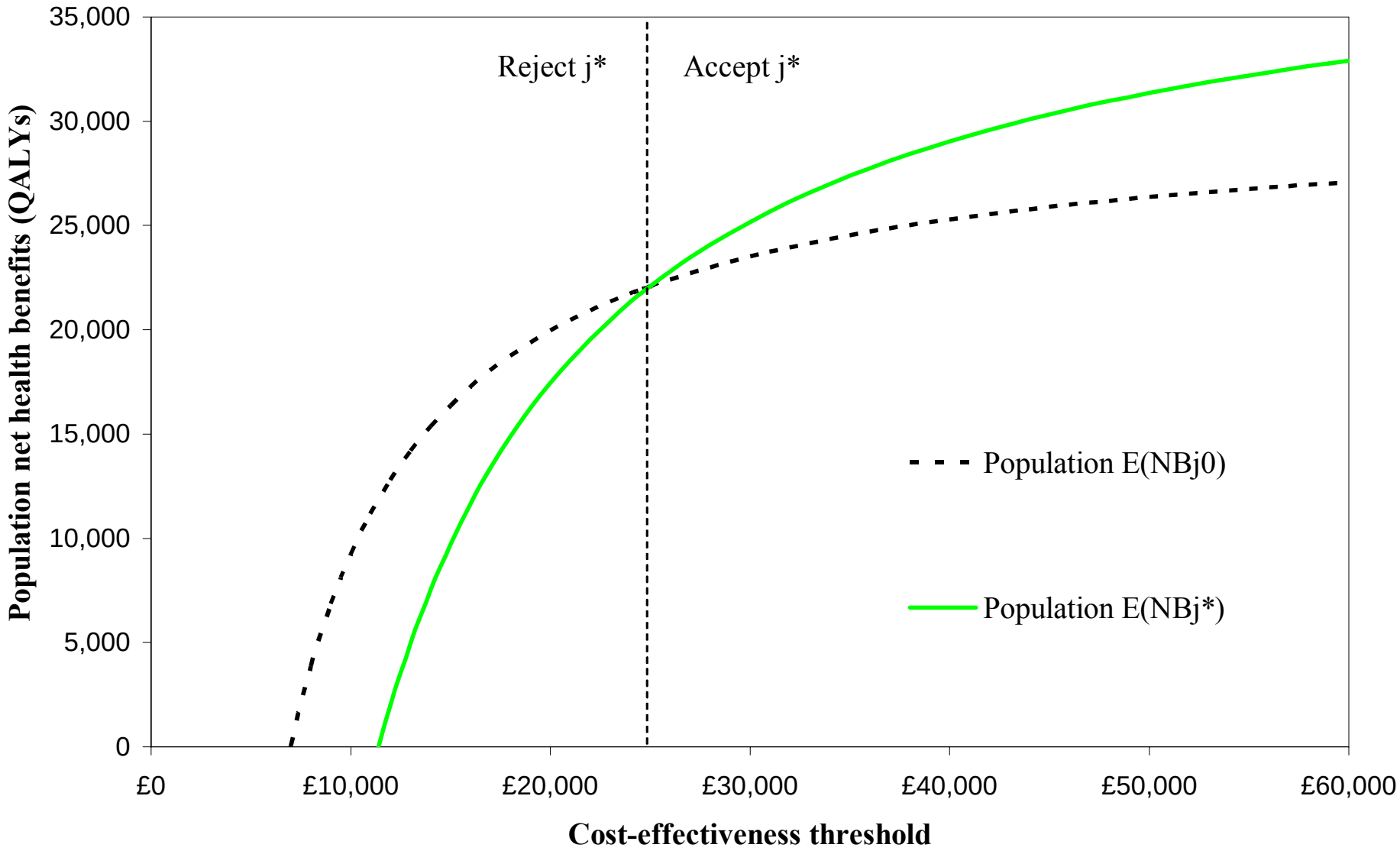
Assume NB is function of uncertain parameters, θ

The irrelevance of inference

- Decision made before it is known how uncertain parameters in the model, θ, resolve.
- With current information should adopt technology that maximises expected NB

$$\max_j E_\theta NB(j, \theta)$$

- Failure to adopt simply because differences in NB are not regarded as statistically significant will impose opportunity costs on patients who could benefit


35,000
30,000
25,000
20,000
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0
Population net health benefits (QALYs)
Reject j*
Accept j*
Population E(NBj0)
Population E(NBj*)
£0
£10,000
£20,000
£30,000
£40,000
£50,000
£60,000
Cost-effectiveness threshold

However....

- Making decisions on expected NB does not mean that uncertainty is irrelevant

- The second question of whether additional evidence is required must be addressed, otherwise:
  - decisions made on limited evidence
  - decisions made on poor quality evidence

The decision to acquire more evidence

- Same objective and conditions as adoption decision
- With decision uncertainty, the technology selected on current evidence may not have maximum NB
  - In these cases patients forgo potential health gains
  - In absence of uncertainty, could always pick technology that maximised health

Expected value of perfect information (EVPI)

- Difference between expected NB of the decision made with perfect information about θ, and the decision made with current information

Expected Value of Perfect Information

- With perfect information can select technology that maximises NB for a particular value of θ
  - true values of θ are unknown

- Expected value of decision with perfect info found by averaging maximum NB over the joint distribution of θ:

$$E\left(NB^{**}\right) = E_{\theta} \max_{j} NB\left(j, \theta\right)$$

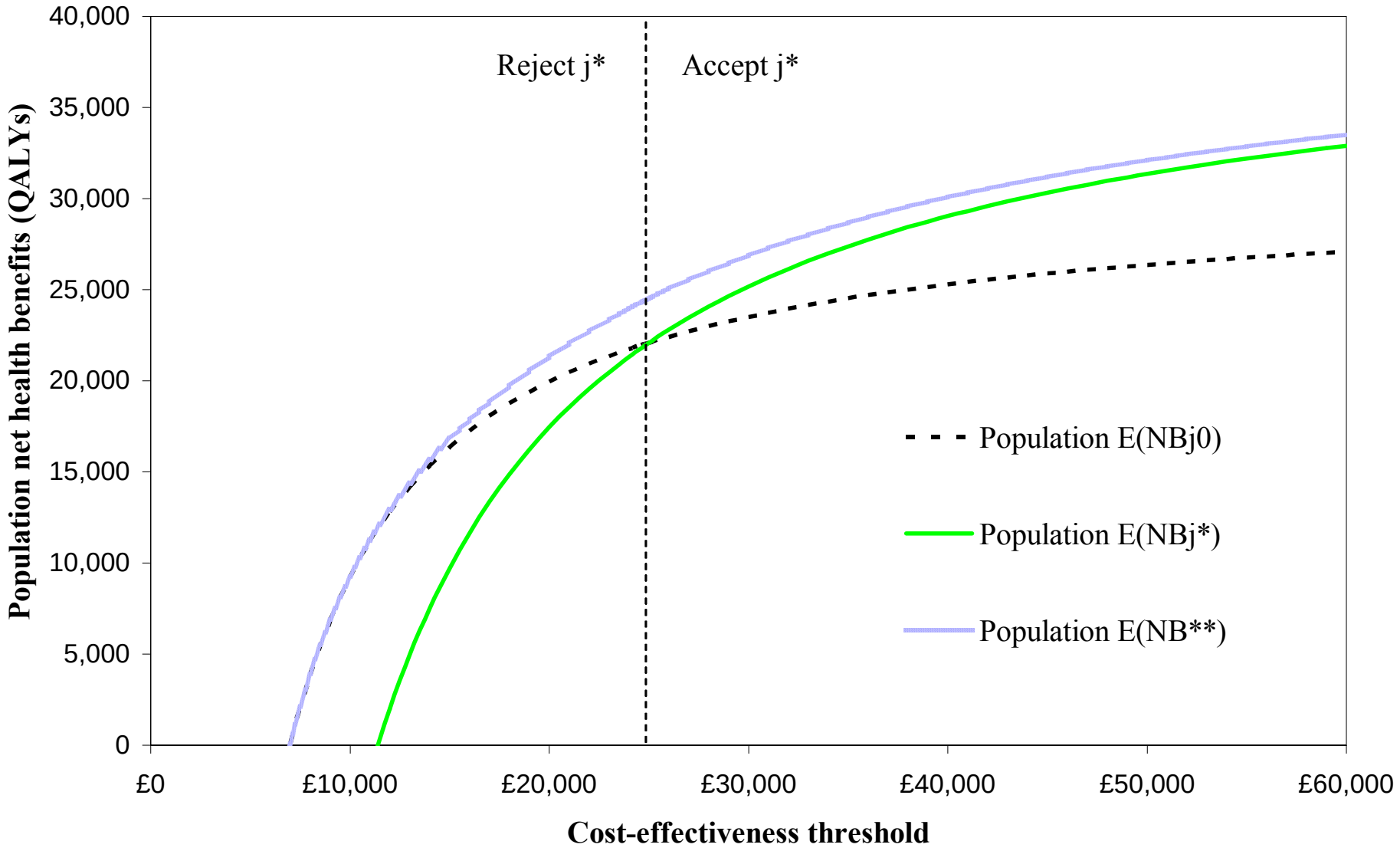
- EVPI is difference between this and expected NB of decision with current info

Population EVPI (and NB)

- Information has public good characteristics
- EVPI for the population based on:
  - Effective lifetime of technology, **T**
  - Incidence over this period, $\mathbf{I_t}$
  - Discount rate, **r**

$$\mathbf{EVPI_{pop} = EVPI.} \sum_{t=1}^{T} \frac{I_t}{(1+r)^t}$$

- population EVPI provides upper bound for value of additional research
  - provides necessary condition for additional research
  - $EVPI_{pop}$ must exceed costs of further investigation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£60,000
Cost-effectiveness threshold
Population E(NBj0)
Population E(NBj*)
Population E(NB**)

The policy environment

Background

- Economic evaluation increasingly used to inform reimbursement/adoption decisions made by funders of health care
  - For example

UK

NHS
National Institute for Health and Clinical Excellence

Canada

Canadian Agency for Drugs and Technologies in Health

Australia

PHARMAC
Pharmaceutical Management Agency

Sweden

LFN
Läkemedelsförmånsnämnden

The policy environment

- Institutions with remit for making adoption decisions often separated from those responsible for prioritising and commissioning research
  - cannot directly arrange funding for research
  - cannot issue/enforce conditional approval

- In these circumstances the adoption decision is the only policy instrument available
  - not clear that question of whether further evidence needed is being addressed simultaneously and consistently

Expected NB decision-making

- Decisions can continue to be based on expected NB if the prospects of further research are unaffected by the adoption decision

- However this is unlikely because:
  - adoption removes incentives for manufacturer of technology to conduct further research
  - diffusion of technology, particularly when mandatory, means future clinical trials less likely to be supported or regarded as ethical
  - adoption can damage recruitment to ongoing trials

Implications

- Adoption can remove an option to acquire additional evidence
- The opportunity loss of adopting a technology can be measured by the value of information that may be forgone
  - this opportunity loss could be greater than the net benefits offered by the technology
- If reimbursement authorities are not given remit to commission/demand research then may be better to deny approval of apparently cost-effective technology

Calculating the opportunity losses of adoption and rejection

Context

- Decision maker whose role is limited to granting approval for reimbursement of mutually exclusive alternatives, j
- New technology, j^*, has greater expected NB than current practice, j_0

- To estimate value of information forgone need assessments of:
  - Probability that research will be conducted, α
  - Time at which research will report, τ

Population to benefit

- Split future patient population into
  - Those who benefit from treatment decision based on current evidence:

$$P_{t<\tau} = \sum_{t=1}^{\tau} \frac{I_t}{(1+r)^t}$$

  - Those who can benefit from decision incorporating results from further research:

$$P_{t>\tau} = \sum_{t=\tau}^{T} \frac{I_t}{(1+r)^t}$$

Expected net benefits of rejection

- If approval of **j*** is withheld, patients receive **j_0** and the associated NB, **$E_\theta\, NB(j_0,\theta)$**
- If research conducted and reports at time, τ, decision can be revised and the maximum future patients will receive is **$E_\theta \max_j NB(j,\theta)$** :
- The expected net benefits of rejecting j* are then:

$$B_R = E\left(NB_{j^0}\right)\cdot P_{t<\tau} + \left(1-\alpha_R\right)\cdot E\left(NB_{j^0}\right)\cdot P_{t>\tau} + \alpha_R \cdot E\left(NB^{**}\right)\cdot P_{t>\tau}$$

Expected net benefits of adoption

- Patients receive j* and the associated net benefits, E_θ **NB(j*,θ)**

- If research conducted and reports at time, τ, decision can be revised and the maximum future patients will receive is $E_\theta \max_j$ **NB(j,θ)** :

- The expected net benefits of adopting j* are then:

$$B_A = E\left(NB_{j^*}\right)\cdot P_{t<\tau} + \left(1-\alpha_A\right)\cdot E\left(NB_{j^*}\right)\cdot P_{t>\tau} + \alpha_A \cdot E\left(NB^{**}\right)\cdot P_{t>\tau}$$

Condition for immediate adoption

- Benefits of adoption should exceed benefits of reject:

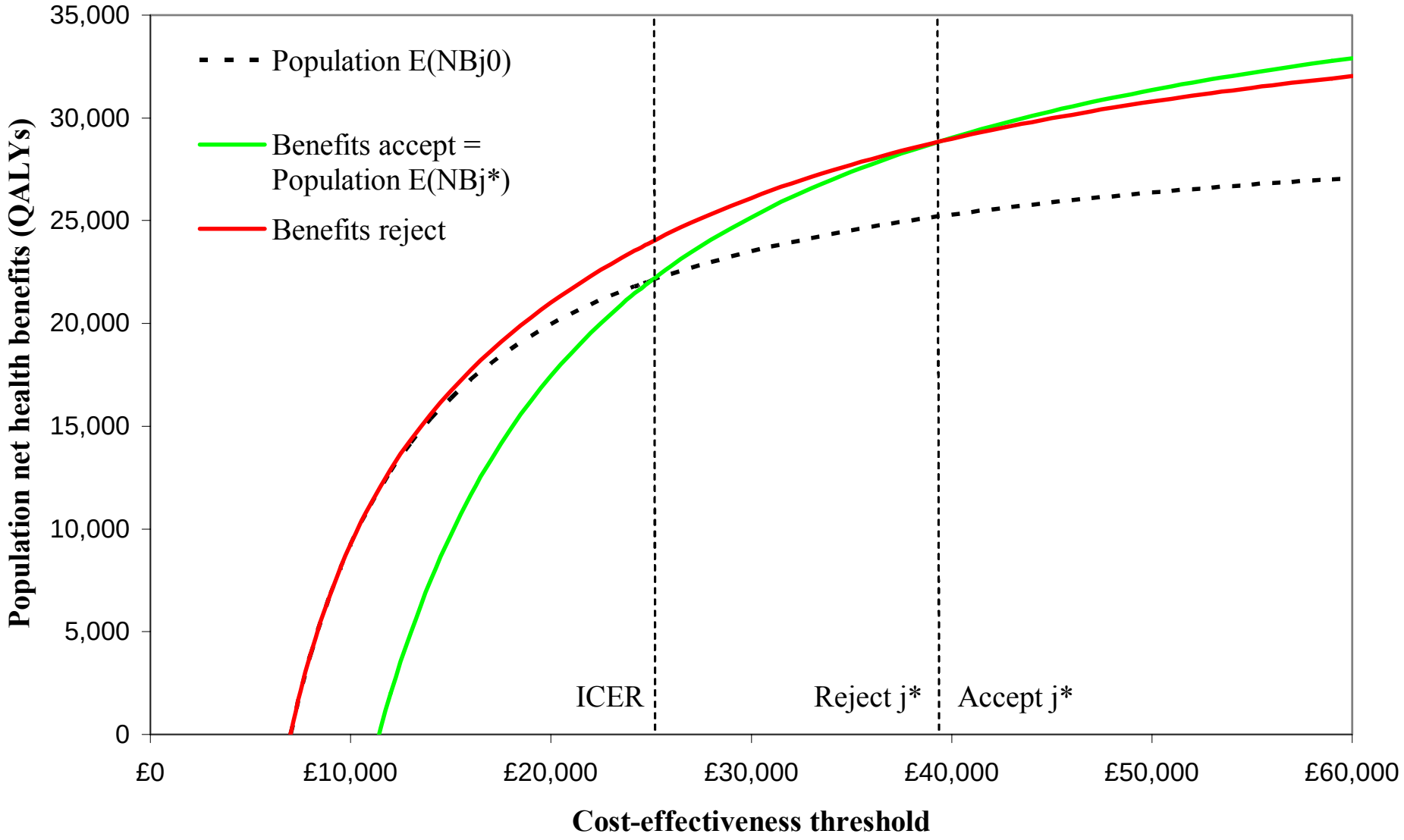
$$B_A - B_R = \left[E\left(NB_{j^*}\right) - E\left(NB_{j^0}\right) \right] \left(P_{t<\tau} + \left(1-\alpha_R\right) P_{t>\tau} \right) - \left(\alpha_R - \alpha_A\right) \left[E\left(NB^{**}\right) - E\left(NB_{j^*}\right) \right] P_{t>\tau}$$

- Standard condition for adoption is special case
  - Adoption does not affect prospects for research, $\alpha_A = \alpha_R$
  - Approve if $E\left(NB_{j^*}\right) \geq E\left(NB_{j^0}\right)$

New decision rule

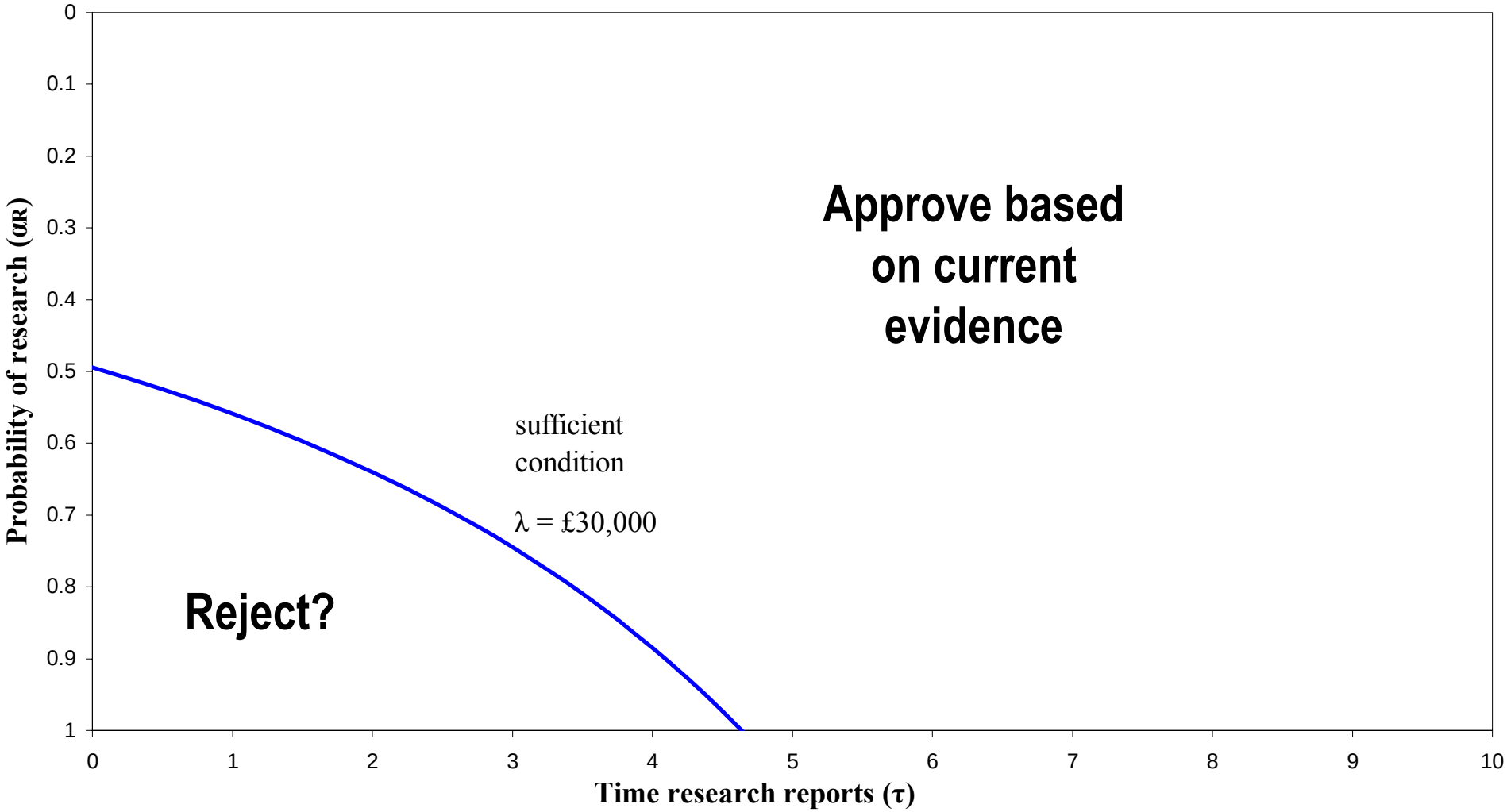
Examples

- Will now demonstrate:
  - Difference with decision making based on expected NB
  - Incentives offered by decision rule that incorporates opportunity cost of research forgone
    - Price
    - Uncertainty
  - Implications for different types of research



$$\alpha_R = 1 \quad \alpha_A = 0 \quad \tau = 2$$

Combinations of α_R and τ for which $B_A = B_R$

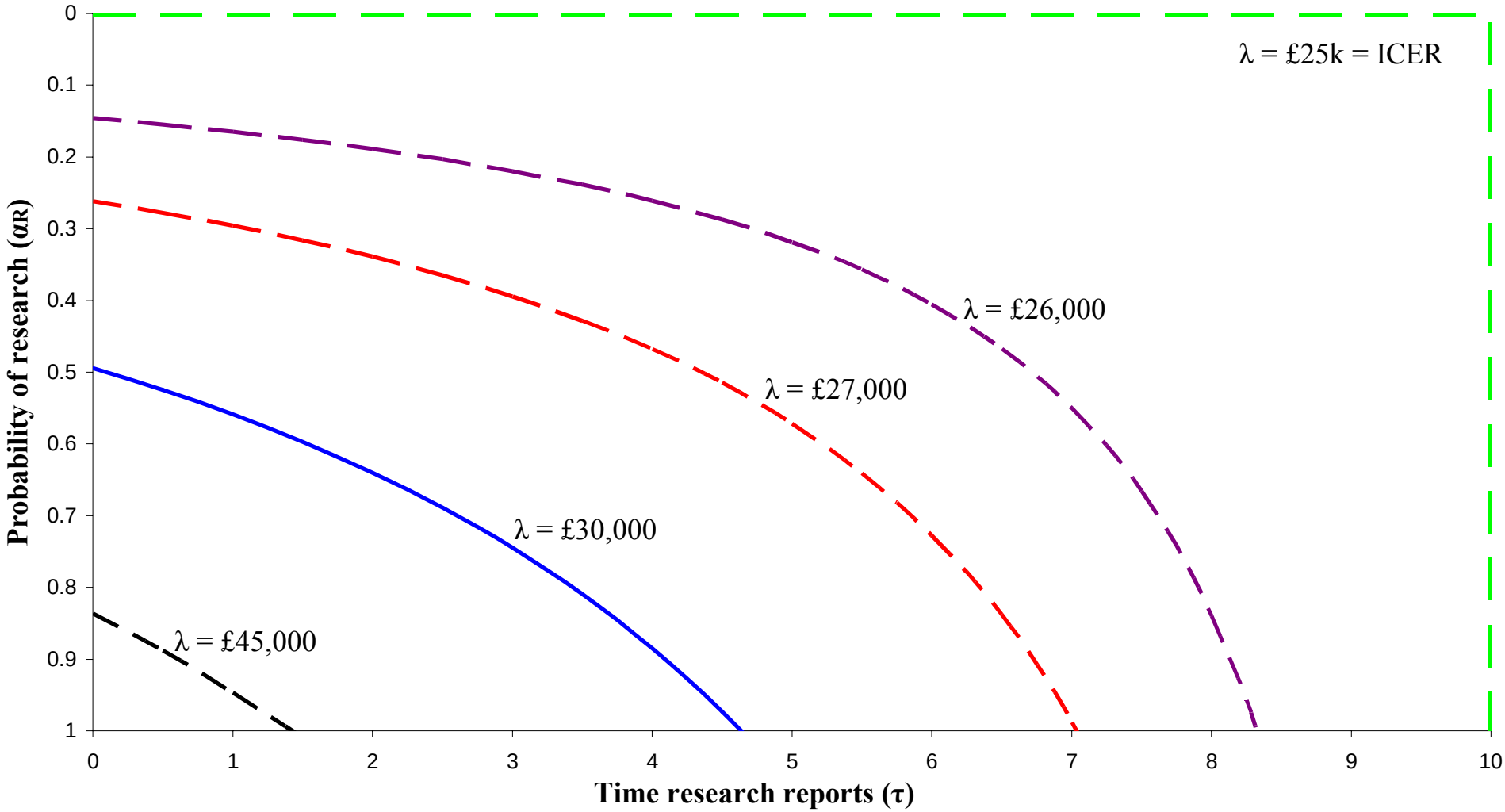


$$\alpha_A = 0$$

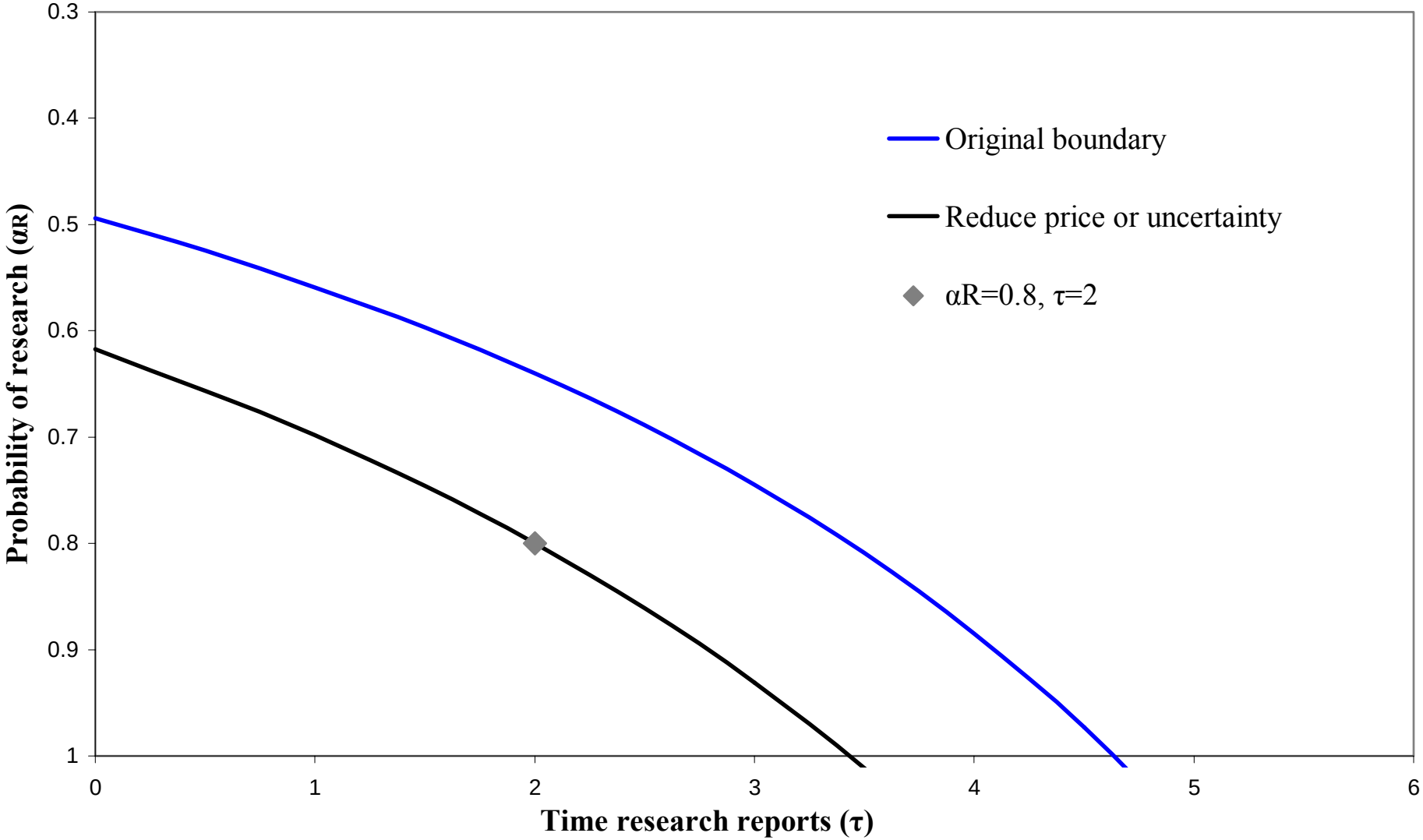
The decision to adopt

- Technologies for which research prospects lie to the north-east of the boundary should be approved
- Technologies that lie to the south-west may require further consideration
- Boundary based on value of perfect info
  - Boundary based on sample info lies to south-west
  - Computationally expensive to assess EVSI
  - However, given α and τ can calculate threshold for EVSI as a guide

Impact of the threshold on the boundary for approval



Impact of the price and uncertainty on the boundary for approval



Impact of price and uncertainty

- Reducing price increases the benefits of immediate adoption, $\mathbf{E_\theta\, NB(j^*,\theta)}$
  - If uncertainty associated with incremental cost, reducing price also reduces value of information
- Reducing uncertainty reduces the value of any information forgone by immediate adoption
- Reducing price or uncertainty will in most cases increase B_A-B_R

Incentives to manufacturers

To review:

- Decision rules based solely on expected NB
  - set price so that ICER just below threshold
  - thus minimising R&D costs and capturing surplus

- Decision rules that consider the opportunity loss of adoption
  - provide more evidence to support technology
  - reduce price

What type of research?

Research decision space

- Different parameters contribute to overall decision uncertainty
  - Type of evidence determines appropriate research design
  - Different research designs affected in different ways by adoption
- Suppose $\theta_1, \theta_2 \cup \theta$
  - If θ_1 relative effect of j* $\rightarrow$ RCT; $\alpha_R^{\theta 1} > \alpha_A^{\theta 1} = 0$
  - If θ_2 quality of life $\rightarrow$ observational study; $\alpha_R^{\theta 2} = \alpha_A^{\theta 2}$
  - Time to research $\tau_{\theta 1} > \tau_{\theta 2}$

Uncertainty in α and τ

- Characterise uncertainty associated with τ and α by assigning appropriate prior distributions
  - allows calculation of expected payoff from immediate adoption, $E(\Pi_A)$

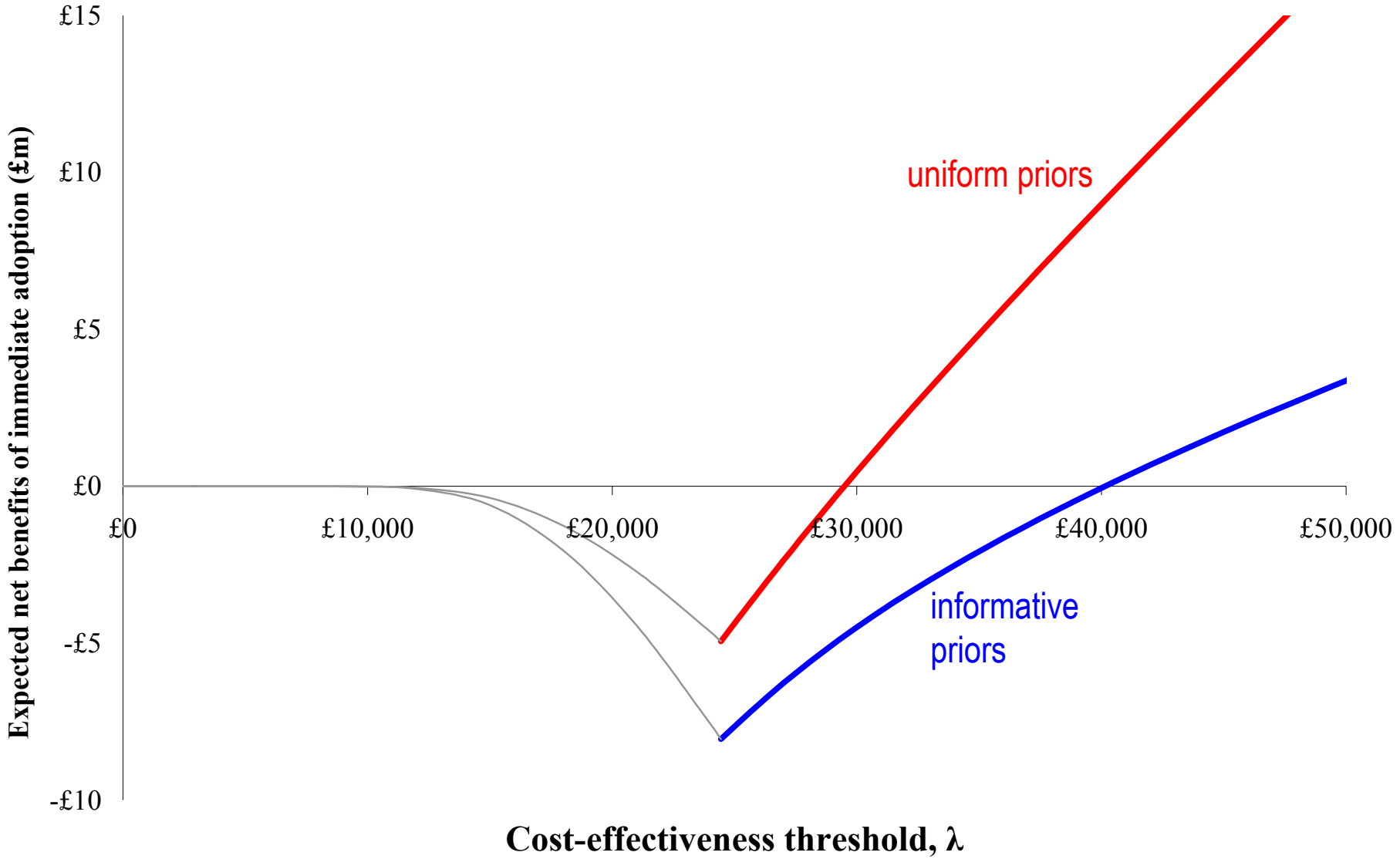
- For example:
  - trial registry indicates ongoing trial
  - protocol indicates when results expected to be reported

    $\tau \sim gamma(25,0.1);$ $\alpha \sim beta(2.4,0.6)$

  - no information about potential further research

    $\tau \sim unif(0,T);$ $\alpha \sim unif(0,1)$

Figure 5. Expected net benefits of immediate adoption



Discussion

Recap

- If objective is to maximise health gains from available resources
  - has been argued that decision to adopt be based on expected cost, expected outcomes and an assessment of the cost-effectiveness threshold
- However this is only justified
  - if question of whether additional evidence required assessed simultaneously
  - or adoption decision does not affect prospects for future research

Recap

- Adoption decision is likely to affect prospects for further research
  - adoption decision cannot be separated from question of whether evidence is sufficient
  - not clear whether this is recognised in current policy environment
- Where adoption decision only policy instrument
  - adoption decision cannot be based on expected NB
  - require assessment of opportunity loss of immediate adoption

Benefits of formal approach

- Have demonstrated formal framework for evaluating the opportunity losses
  - provides incentives for manufacturers to reduce price or provide additional evidence
- Current 'informal' approach
  - lack of legal standing to back-up recommendations
  - not transparent
    - problems with consistency, predictability, incentives

Other issues

- Rely on EVPI and assessment of threshold for EVSI
- Consider only current decision problem
  - value of additional information may be underestimated