New drugs in lymphoma treatment: Economic sustainability

Claire Rothery, PhD

Centre for Health Economics, University of York, UK

Outline

- Economic evaluation for resource allocation decisions in health care
- Decision rules used in cost-effectiveness analysis
- Case study from UK NICE Appraisal process: Obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia

Making choices based on economic criteria

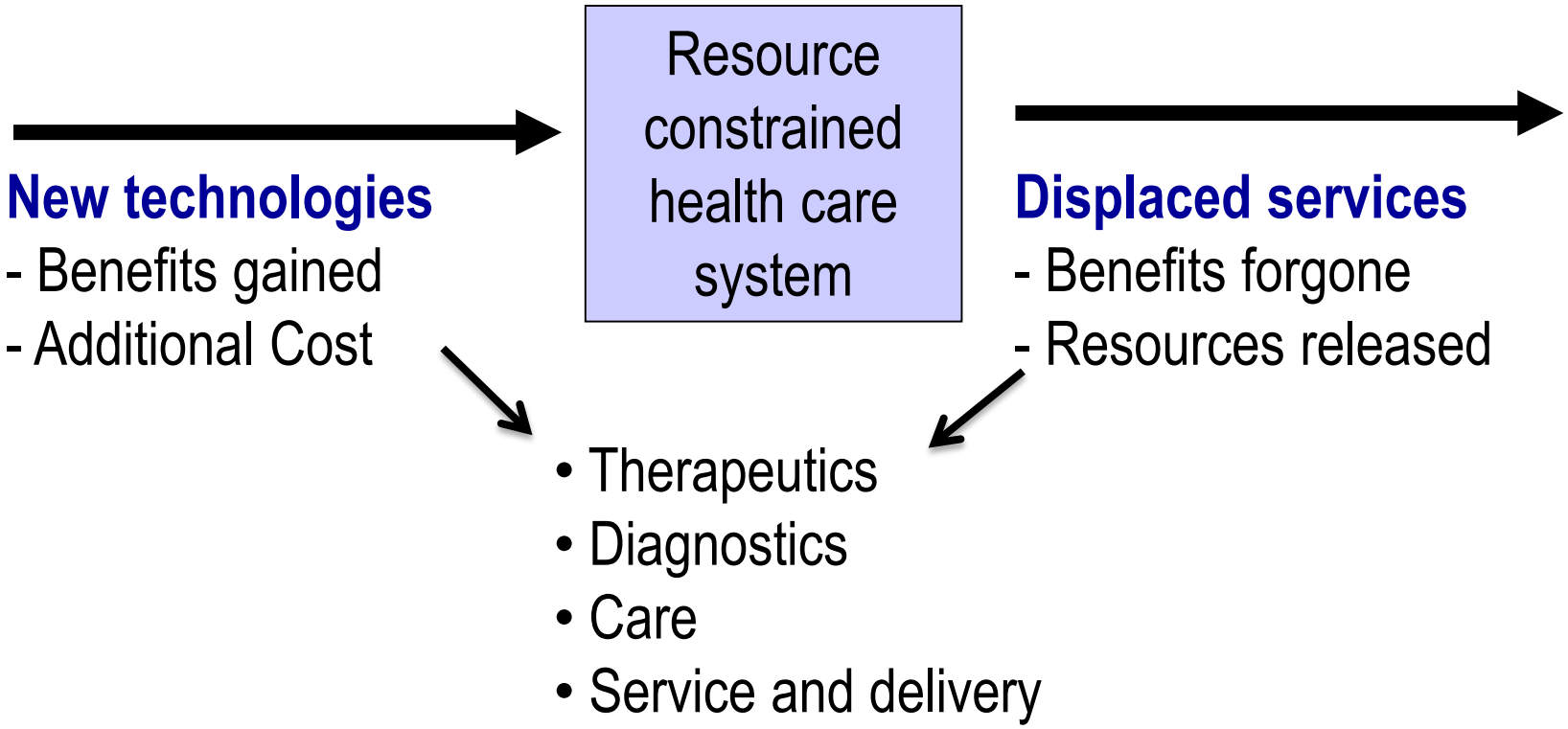
- All collectively funded health care systems (whether predominantly tax-based, social insurance or mixed) need to **make choices about the allocation of resources**

- The underlying problem is one of **limited resources**, **unlimited 'wants'**
  - Not everything that offers a benefit can feasibly be funded
  - Choices need to be made between alternative uses of resources

- Decision maker's objective is to ensure that a particular programme represents an efficient use of healthcare resources

→ Choose programmes which **maximise total health benefits subject to the budget constraint** (resource constraints)

The challenge of health care decisions



Is the benefit gain from the new treatment greater than the benefit foregone through displacement?

Opportunity cost

You can spend £1, $1 or €1 only once

Within a fixed budget constraint, if the healthcare system spends more on one thing, it has to do less of something else

The **opportunity cost** is the value of the next best alternative use of resources

Source: Peter Littlejohns, The Challenge of Health Care in Europe: “value for money”

Cost-effectiveness analysis (CEA)

- Focuses on the **health** of the **population**
- There are different forms of economic evaluation but the most common method used for resource allocation in health care is **CEA**
- Involves the **comparative** analysis of alternative courses of action in terms of both their **costs** and their **health outcomes**
- **Costs** include direct and/or indirect costs

Direct costs

Health services resource use
- Inpatient stay, outpatient visits,
- Tests,
- Drugs
- GP, nurse, consultant time
- Equipment space/facilities

Indirect costs

Wider costs to society
- Productivity losses

Patient and family costs
- Out of pocket expenses
- Carer time

'Give it to me straight, doc, how long will my car have to spend in the hospital car park?'

Health outcomes

- Disease specific outcomes - focuses on health outcomes specific to an individual disease, an identified population

- Limitations → Not a comprehensive measure of health & QoL

  Narrow focus on disease endpoints, clinical significance unclear *(e.g. cost per toenail fungal infection averted)*

- Health outcomes are measured using generic measures:

  Physical and social functioning, pain, psychological well-being, vitality

- **Quality-adjusted life years (QALYs)** represent health on a scale from 0 (death) to 1 (full health); generally measured using public preference values over health states

- Comparison across different health care programmes

  Priority setting in health care (opportunity cost) → Compare added QALYs with QALYs lost from displaced programmes

Using CEA to inform decision making

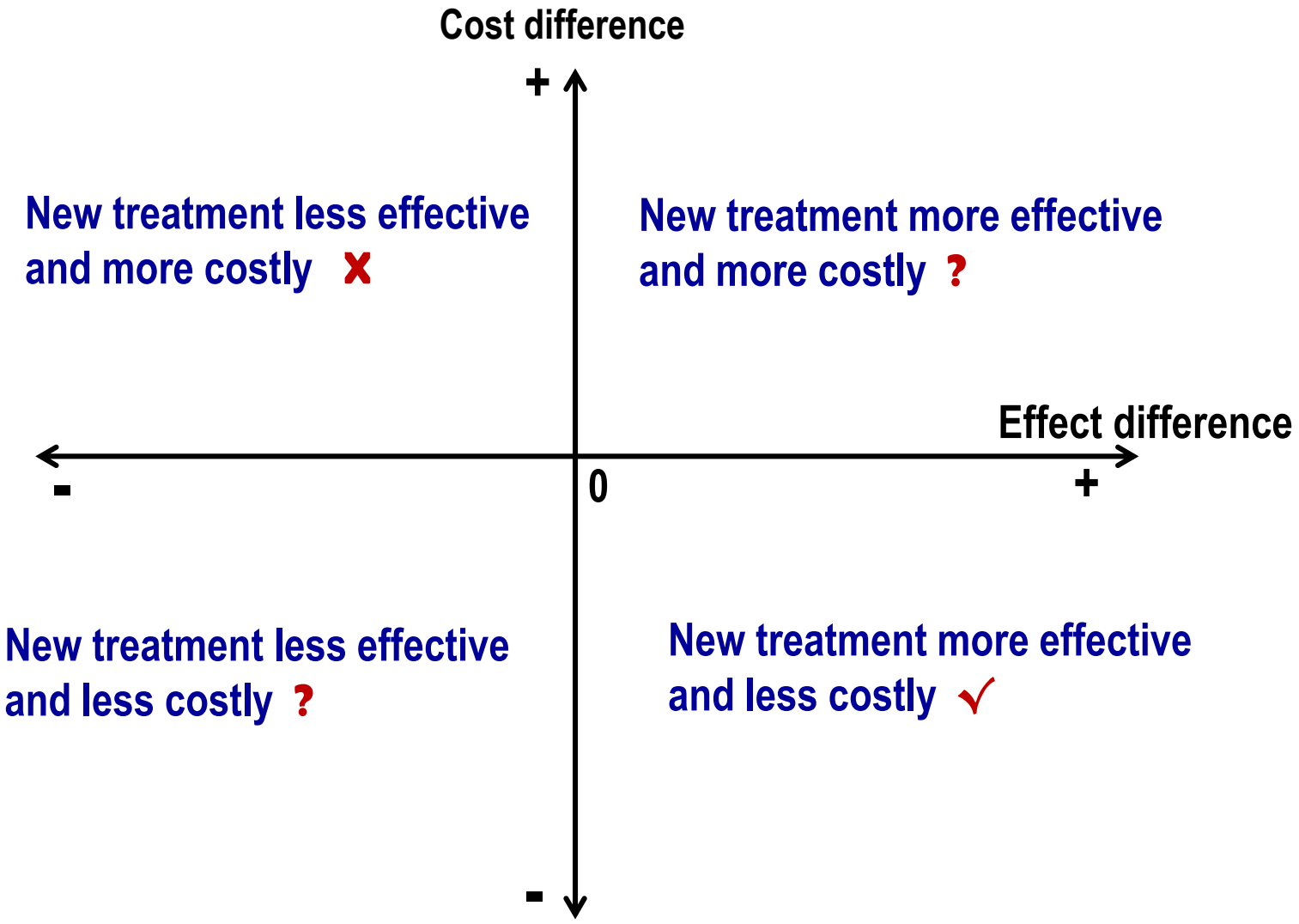
- Assess what *extra* benefits we incur for any *extra* costs

- The traditional analytic tool of cost-effectiveness analysis is the **incremental cost-effectiveness ratio (ICER)**

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{\text{Cost of new treatment} - \text{cost of standard treatment}}{\Delta E = \text{Effect of new treatment} - \text{effect of standard treatment}}$$

→ **ICER = Cost per QALY gained**

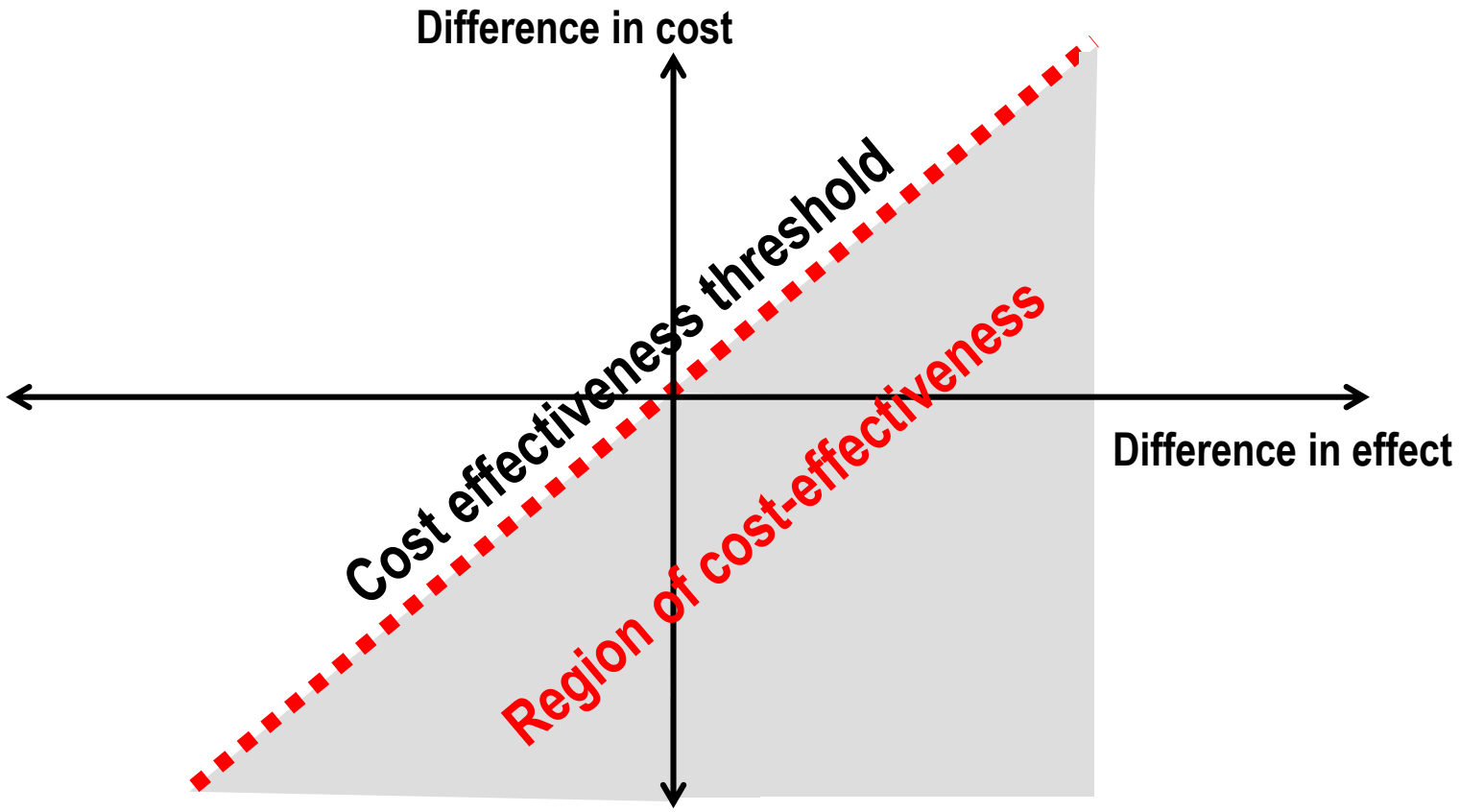
Cost-effectiveness plane



Cost effectiveness decision rules

The league table rule: Select programmes in ascending order of the ICER until resources are exhausted

The threshold rule: Select programmes with **ICER ≤ Threshold**



How UK NICE says it makes decisions:

6.3.3 Above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of the technology as an effective use of NHS resources will specifically take account of the following factors:

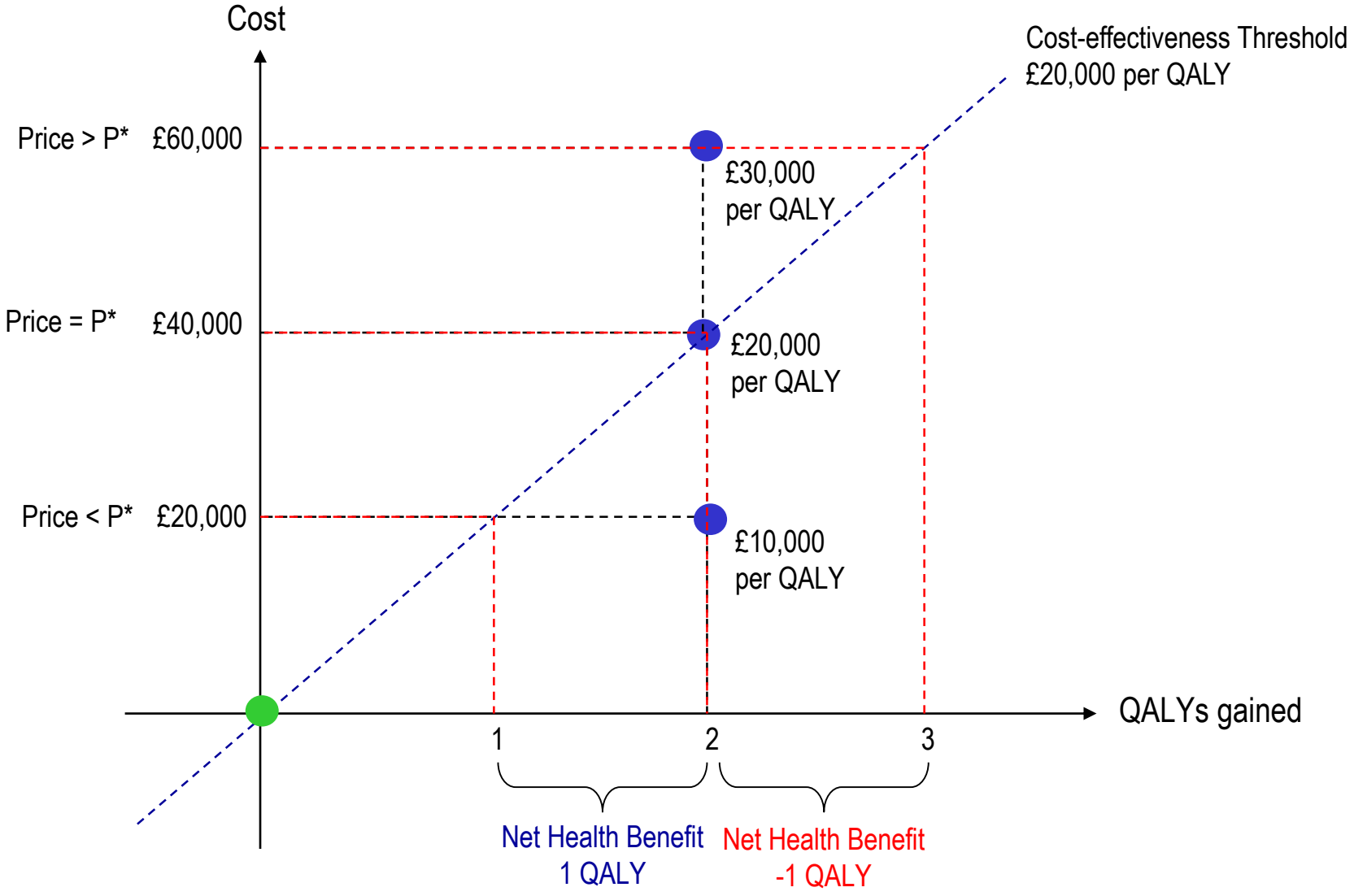
- The degree of certainty around the ICER. In particular, the Committee will be more cautious about recommending a technology when they are less certain about the ICERs presented.
- Whether there are strong reasons to indicate that the assessment of the change in health-related quality of life has been inadequately captured, and may therefore misrepresent the health utility gained.
- The innovative nature of the technology, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the reference case QALY measure.
- The technology meets the criteria for special consideration as a 'life-extending treatment at the end of life' (see section 6.2.10)
- Aspects that relate to non-health objectives of the NHS (see sections 6.2.20 and 6.2.21).

6.3.4 As the ICER of an intervention increases in the range of £20,000 to £30,000 per QALY gained, the Committee's judgement about the acceptability of the technology as an effective use of NHS resources will make explicit reference to the relevant factors listed in section 6.3.3.

6.3.5 Above a most plausible ICER of £30,000 per QALY gained, the Committee will need to identify an increasingly stronger case for supporting the technology as an effective use of NHS resources, with regard to the factors listed in section 6.3.3.

Source: National Institute for Health and Care Excellence (NICE). *Guide to the Methods of Technology Appraisal*. London: NICE, 2013.

What does the threshold mean?



Claxton et al. *British Medical Journal* 2008;336:251-4.

UK National Institute for Health and Care Excellence (NICE)

http://www.nice.org.uk/

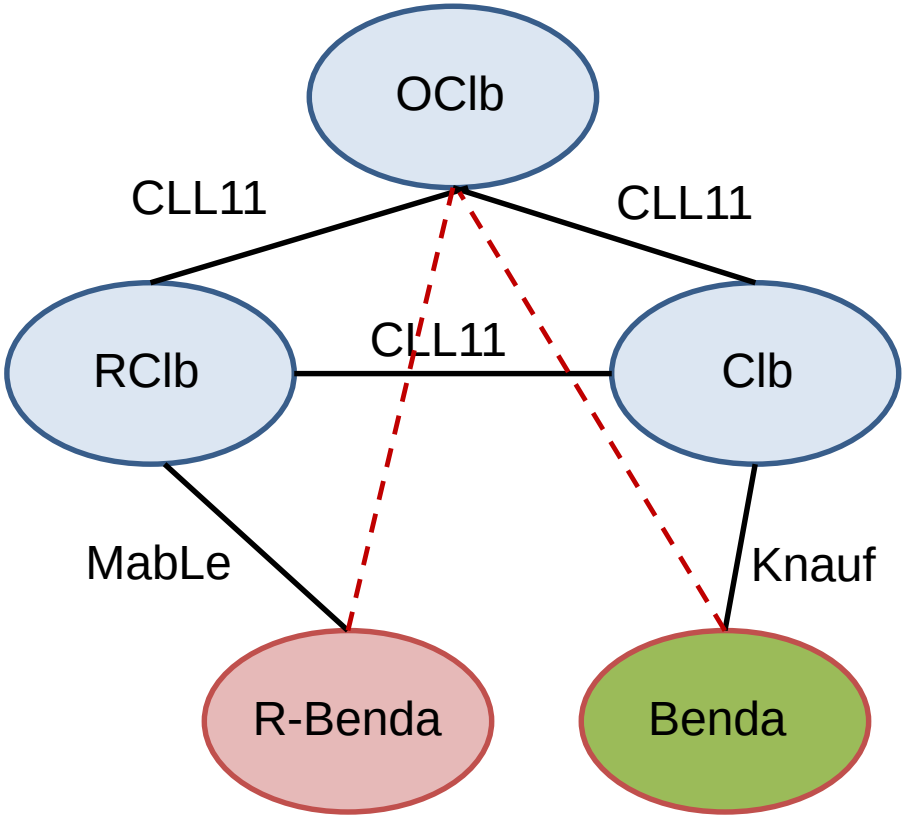
Obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia

Decision problem

Manufacturer's decision problem	
Population	Adults with previously untreated CLL for whom full-dose fludarabine-based therapy is inappropriate
Intervention	Obinutuzumab in combination with chlorambucil (OClb)
Comparators	Chlorambucil (Clb); Bendamustine (Benda); Rituximab + chlorambucil (RClb); Rituximab + bendamustine (RBenda)
Outcomes	Progression-free survival (PFS); Overall survival (OS); Response rates; Adverse effects of treatment; Health-related quality of life (HRQoL)
Economic analysis	Perspective for costs was health service Time horizon is lifetime (20 years) Costs and benefits discounted at 3.5% per annum

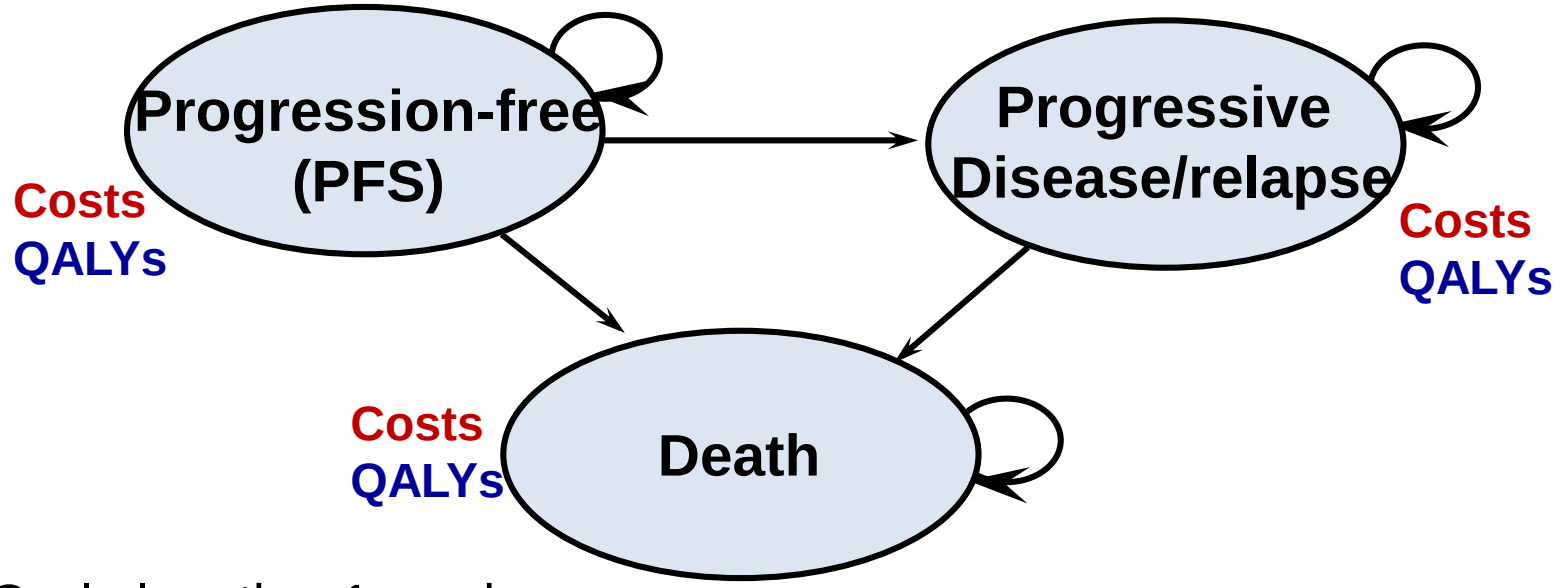
Evidence on effectiveness

- Efficacy and safety from 3-arm RCT trial (**CLL11 trial**):
  obinutuzumab + chlorambucil (OClb) compared with
  - rituximab + chlorambucil (RClb)
  - chlorambucil alone (Clb)
- Primary end point was progression-free survival (PFS). Secondary outcomes included overall survival (OS)



Network meta-analysis
for comparison with
- rituximab + bendamustine
- bendamustine

Decision model for costs and health outcomes

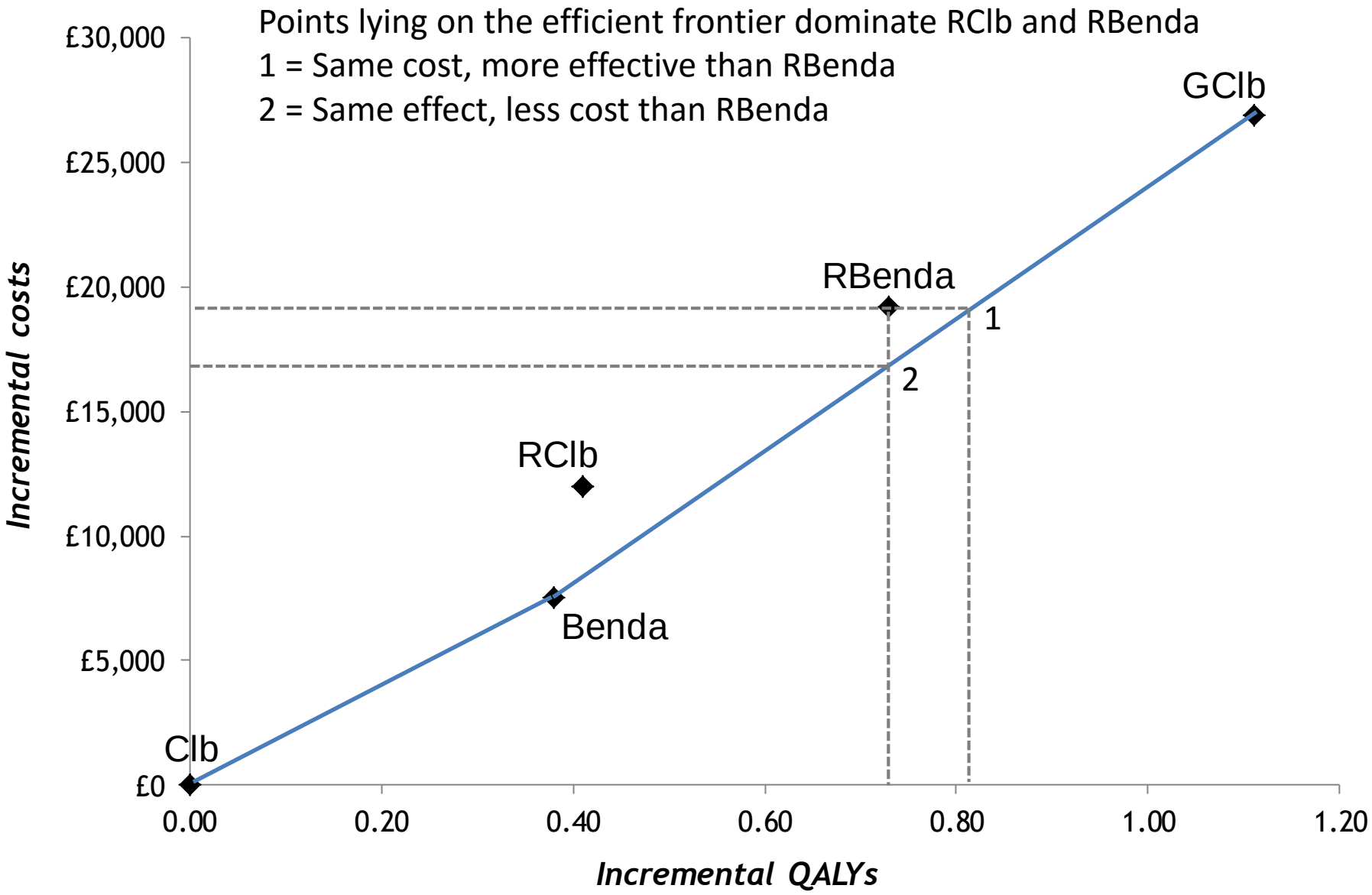


- Cycle length – 1 week
- Time in PFS state = PFS curve of CLL11 trial + extrapolation
- Time in progressed state = Time in OS curve – proportion in PFS
- Costs: Drug costs, administration, haematologist consultation time, pharmacy time, follow-up visits with haematologist by state, adverse events
- QALYs: EORTC-QLQ-C30 mapped to EQ-5D, health state, adverse events

Manufacturer's cost-effectiveness results

	Total costs	Total QALYs	Incr. costs	Incr. QALYs	ICER	Dominated?
Clb	£8,020	2.92				
Benda	£15,557	3.30	£7,536	0.38	£19,983	N
~~RClb~~	~~£20,002~~	~~3.33~~	~~£4,445~~	~~0.03~~	~~£144,269~~	~~Y – ED~~
~~RBenda~~	~~£27,215~~	~~3.65~~	~~£7,213~~	~~0.32~~	~~£22,718~~	~~Y – ED~~
OClb	£34,888	4.03	£7,673	0.38	£20,076	N

Cost-effectiveness efficiency frontier



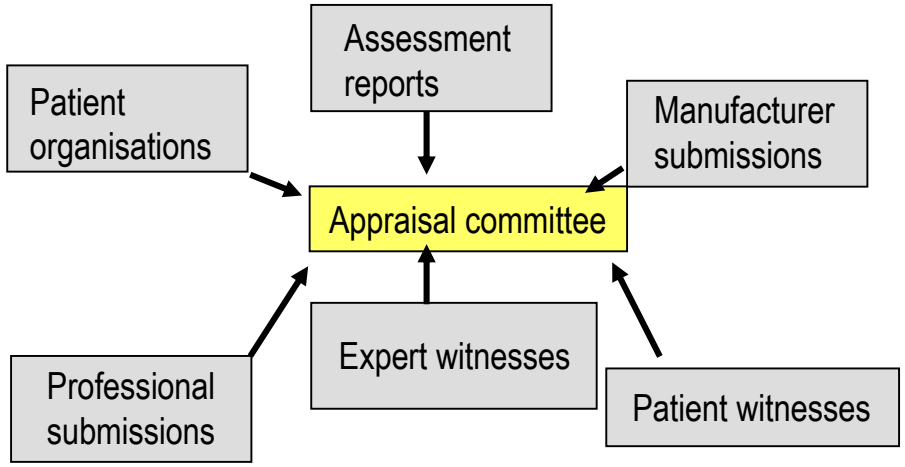
Manufacturer's cost-effectiveness results

Incremental cost-effectiveness results:

	Total costs	Total QALYs	Incr. costs	Incr. QALYs	ICER
Clb	£8,020	2.92			
Benda	£15,557	3.30	£7,536	0.38	**£19,983 (vs. Clb)**
OClb	£34,888	4.03	£19,331	0.73	**£26,463 (vs. Benda)**

Other considerations:

- Academic critique and analysis
- Uncertainty in the evidence
- Innovation
- End of life
- Equality
- Patient access scheme



Obinutuzumab + chlorambucil is recommended (with some restrictions)

Summary

- Economic sustainability of new drugs involves assessing the opportunity cost
  - What existing treatments will have to be displaced?
  - What resources will be released?
  - What health benefits will be forgone?

- A rule of thumb
  - Does the extra cost of a unit of benefit compare when with previous decisions?

- What is society willing to pay for an extra unit of benefit?
  - Increase insurance premiums/taxation to provide new intervention