Trends in the Use of Economic Data in Drug Reimbursement Decisions

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SOME BACKGROUND

- Several countries now require economic data for drug reimbursement decisions, the ‘so called’ Fourth Hurdle.
- NICE, in England and Wales, has been widely discussed, but is now changing many of its procedures.
- Other large countries, such as Germany through IQWiG, are adopting the approach.
- Even in the USA, there are signs of a growing importance of economic data (e.g. CMS, Wellpoint).

CURRENT ISSUES

- Are additional countries introducing a requirement for economic data?
- Are assessment procedures changing?
- How is methodological development progressing (or regressing)?
- Is there more international collaboration, or convergence of approaches?
- On balance, is life getting easier or harder for industry?

DEVELOPMENTS IN NICE's PROCEDURES

- Single Technology Appraisals.
- Stakeholder Involvement.
- Scoping Workshops.
- Methodological Developments.
- International Convergence.

NICE'S SINGLE TECHNOLOGY APPRAISALS

- A new 'fast track' procedure introduced in response to concerns over the time taken by NICE's standard approach.
- So far applies to drugs, in the main cancer drugs.
- Places more emphasis on analyses submitted by the manufacturer and incorporates less external review.

NICE'S SINGLE TECHNOLOGY APPRAISALS

- May suffice in situations where the number of comparators is limited.
- Raises further questions about the methods for prioritising topics.
- Raises issues about burden of proof and responsibility for the results of the appraisal.
- Not necessarily an easier process for the manufacturer.

ASSESSMENT PROCEDURES

- The majority of HTA agencies undertake assessments in-house, although probably all commission some work outside (e.g. in Canada, CCOHTA spends 25% of its budget outside).
- In England, NICE places considerable emphasis on independent review by academic groups.
- By-and-large the independent review groups apply ‘Cochrane-style’ methods.

IS INDEPENDENT REVIEW COST-EFFECTIVE?

- Re-affirms the ‘arms length’ nature of HTA (assessment ≠ appraisal).
- More transparent and may help resolve disputes when multiple products are being considered.
- The Scots claim they reach the same decisions at a fraction of the (assessment) cost, but other analyses show differences between SMC and NICE decisions.
- Systematic reviews place emphasis on RCTs as compared with other study designs.
- Sometimes the economic model does not follow from the systematic review (‘a game of 2 halves’).

REASONS FOR NOT USING THE SYSTEMATIC REVIEW IN THE ECONOMIC EVALUATION

- NICE likes to see QALYs.
- Preference-based QoL measures are only occasionally used in clinical studies.
- The summary measure of clinical effectiveness does not facilitate the calculation of QALYs.

EXAMPLES

- *New drugs for epilepsy (adults):*
  - clinical effects assessed in terms of total or partial reduction in seizures;
  - these were classified as partial and total response and a utility value to each state.
- *Drug therapy for attention-deficit hyperactivity disorder (ADHD):*
  - effectiveness measure was points change on the Connors Hyperactivity Scale;
  - economic evaluation used response/non-response and assigned a utility to each state.

STAKEHOLDER INVOLVEMENT

- Stakeholders can include manufacturers, professional organisations, health authorities, academic groups and patient organisations.
- All HTA agencies have some stakeholder involvement, but NICE is probably at the all-inclusive end of the spectrum.
- Stakeholder involvement is resource-intensive but may (i) lead to better assessments; (ii) reduce the number of appeals and (iii) lead to better implementation of HTAs.

SCOPING WORKSHOPS

- Have been a feature of NICE's procedures for around 3 years.
- Useful for determining the technologies to be appraised and the nature of the evidence requirements.
- Provide an opportunity for manufacturers to ask questions of NICE and the evaluation team.
- Probably reduces the arguments at a later stage.

METHODOLOGICAL DEVELOPMENT

- No doubt that HTA processes in the UK have stimulated methodological development; e.g. mixed treatment comparisons; probabilistic models.
- Several methodology TARs.
- The NHS Methodology Programme has a good track record in funding projects relevant to HTA.

MAKING INDIRECT COMPARISONS

- Unless the decision can wait until such studies are available, some modelling/synthesis is required.
- Some studies show a reasonable agreement between head-to-head studies and indirect comparisons, in cases where studies with a common (third) treatment are used (Song *et al,* 2003).
- More complex models can be used when studies with common treatment are not available (e.g. multi-parameter synthesis).

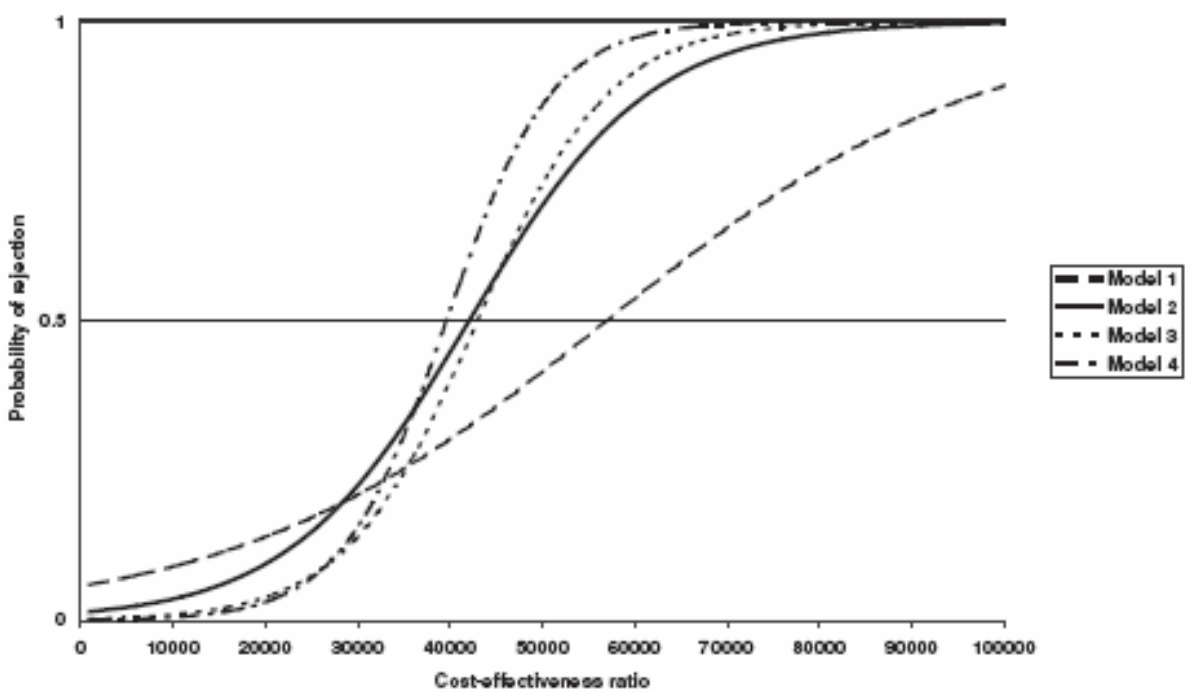
EXTRAPOLATING BEYOND THE DURATION OF CLINICAL TRIALS

- A full economic evaluation requires long-term outcomes (e.g. life-years gained, QALYs gained).
- Normally the decision (on use of the technology) cannot wait until long-term data are available.
- Projections are needed for: (i) maintenance of treatment effect; (ii) rates of withdrawal from therapy; (iii) implications of withdrawal.
- There is no unambiguously right way to make these projections.

CHARACTERISATION OF UNCERTAINTY

- Debate about the need for probabilistic sensitivity analysis (PSA).
- PSA facilitates Value of Information (VOI) analysis, but may limit modelling options.
- Perhaps decision-makers should participate in the debate.

DOES NICE HAVE COST-EFFECTIVENESS THRESHOLD?



Source: Devlin and Parkin. *Health Economics* 2004; 13: 437-452.

ADDITIONAL CONSIDERATIONS IN ESTABLISHING SOCIAL VALUE

- Seriousness of condition.
- Existence of alternative therapies.
- Affordability to patients if not reimbursed.
- Whether a ‘lifestyle’ drug.

INCREMENTAL COST PER ADDITIONAL LIFE-YEAR GAINED LEAGUE TABLE

Number	Incremental cost per additional life-year gained at 1998/1999 prices ($AU)	PBAC decision
1	5517	Recommend at price
2	8374	Recommend at price
3	8740	Recommend at price
4	17387	Recommend at price
5	18762	Recommend at price
6	18983	Recommend at price
7	19807	Recommend at lower price
8	22255	Recommend at price
9	26800	Recommend at price
10	38237	Recommend at price
11	39821	Recommend at price
12	42697	Reject
13	43550	Reject
14	43550	Defer
15	43550	Recommend at price
16	56175	Reject
17	57901	Recommend at price
18	63703	Reject
19	71582	Recommend at price
20	75286	Recommend at price
21	85385	Recommend at lower price
22	88865	Reject
23	98323	Reject
24	229064	Recommend at lower price
25	231650	Reject
26	256950	Reject

$AU = Australian dollars. The average interbank exchange rate to US dollars for 1998/1999 was 0.63772 (range 0.68760 to 0.54850).
PBAC = Pharmaceutical Benefits Advisory Committee.

Source: George *et al*. *PharmacoEconomics* 2001; 19(11): 1103-1109.

SOCIAL VALUE VERSUS COST-EFFECTIVENESS

- Doubts about whether the QALY captures all the elements of social value.
- Other considerations include severity of disease, availability of other therapies and QALYs experienced to date.
- Main issue is whether these considerations should be incorporated into the analysis, or discussed in the committee.
- A recent NICE consultation document on orphan drugs discussed raising the threshold to £200,000 for drugs meeting certain criteria.

DIVERSITY OF INTERNATIONAL REQUIREMENTS

- As more and more jurisdictions request cost-effectiveness data, diversity of requirements becomes a more important issue.
- Some diversity is understandable, but some is not.
- As the requirements for the Fourth Hurdle expand, there should be more discussion of harmonisation of guidelines.

POTENTIAL FOR HARMONIZING INTERNATIONAL GUIDELINES

- As more jurisdictions require economic submissions, the burden on industry increases.
- Local requirements differ, due to a mixture of good and bad reasons.
- There should be potential for more harmonisation.

POSSIBLE INTERNATIONAL REFERENCE CASE

• Study perspective	Health/social care and productivity costs
• Comparators	All relevant comparators
• Source of effectiveness data	Trials and observational studies
• Role of modelling	Essential
• Main economic outcome	QALYs
• Source of utilities	Generic measure
• Characterising uncertainty	One-way sensitivity analysis and summary approach (eg PSA)

CONCLUSIONS

- Assessment procedures are continuing to evolve within NICE.
- With NICE, there seems to be a keenness to stick to the £20,000-£30,000 per QALY threshold.
- There is increasing debate about the difference between cost-effectiveness and social value.
- Methodologies continue to evolve and there is some evidence of international convergence.