Using economic evaluation to inform decisions regarding the adoption of new health technologies

The case of National Institute for Health and Clinical Excellence (NICE) in England

Improving health worldwide

John.Cairns@lshtm.ac.uk

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Outline

- Process
- Assessment of cost-effectiveness
- Developments

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Topic selection
Scoping

	Single Technology Appraisal	Multiple Technology Appraisal
Evidence on clinical and cost-effectiveness	* Company Submission * Evidence Review Group	* Assessment Group * Company Submission

Summary of the clinical & economic evidence by members of committee

Appraisal Committee

Clinical experts
Patient group
Company

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Topic selection
Scoping

	Single Technology Appraisal	Multiple Technology Appraisal
Evidence	* Company Submission * Evidence Review Group	* Assessment Group * Company Submission

Appraisal Committee — Clinical experts, Patient group, Company

Appraisal Consultation Document

Consultation comments → **Appraisal Committee** — Clinical experts, Patient group, Company

Final Appraisal Determination

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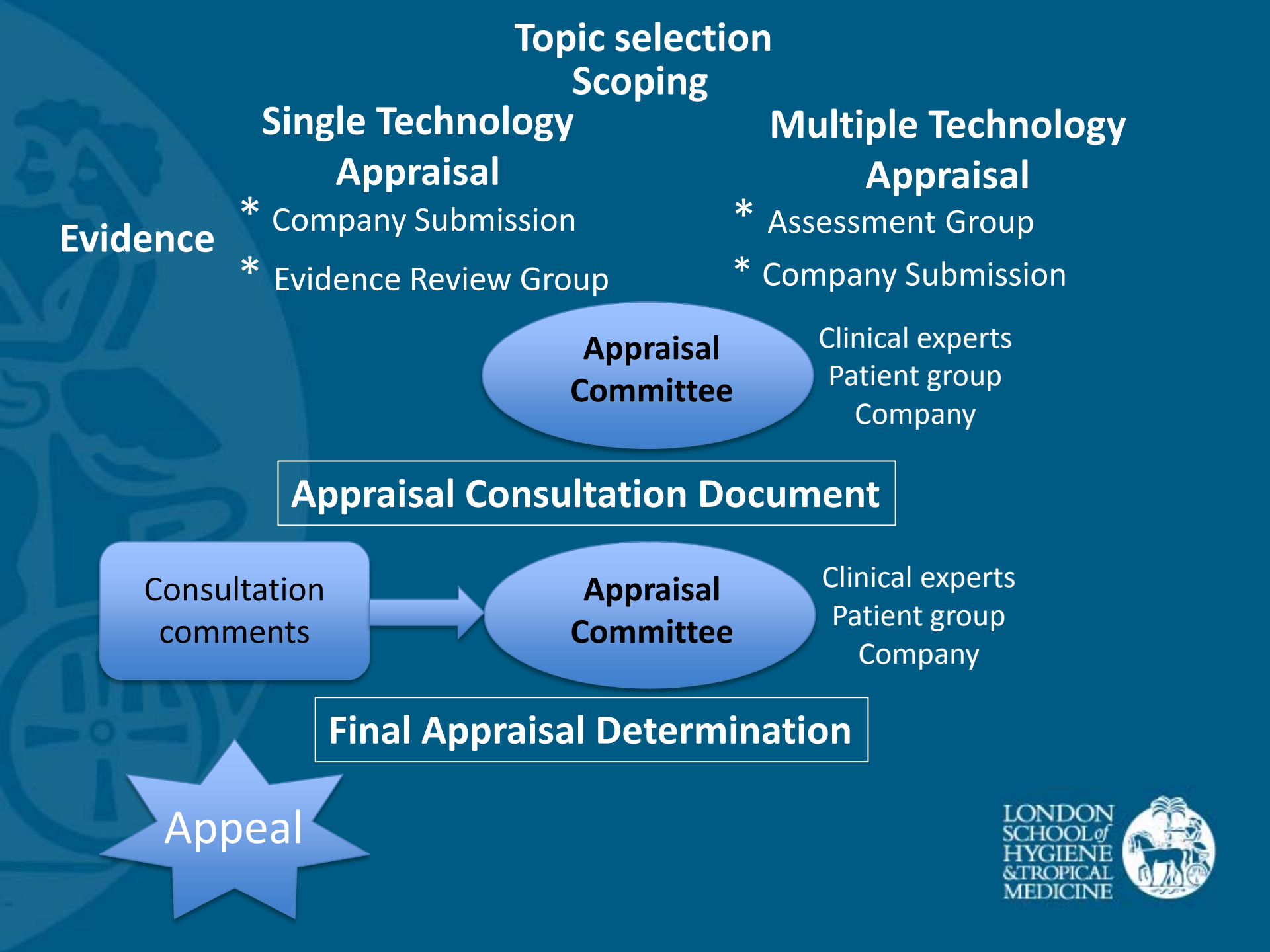
Topic selection
Scoping
Single Technology Appraisal
Multiple Technology Appraisal
Evidence
* Company Submission
* Evidence Review Group
* Assessment Group
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Appraisal Committee
Clinical experts
Patient group
Company
Appraisal Consultation Document
Consultation comments
Appraisal Committee
Clinical experts
Patient group
Company
Final Appraisal Determination
Appeal
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- ❑ Clinical effectiveness and cost-effectiveness
- ❑ Transparent process
- ❑ Highly consultative
- ❑ Relatively slow

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Incremental Cost-Effectiveness Ratio

$$ICER = \frac{COST\ new - COST\ old}{QALY\ new - QALY\ old}$$

Assessment of value is not exclusively driven by cost per QALY but is “based on a deliberative process that also takes into account other factors in order to come to a view on whether or not a treatment is likely to be cost-effective”

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Cost-effectiveness threshold

- "The appropriate threshold to be used is that of the opportunity cost of programmes displaced by new, more costly technologies".
- "Consideration of the cost effectiveness of a technology is a necessary, but is not the sole, basis for decision-making."
- If most plausible estimate is below £20,000 per QALY gained: cost-effective use of NHS resources
- Above £20,000: are there benefits not captured by the QALY? Has quality of life aspect been adequately measured?
- Above £30,000: increasingly less likely to recommend the technology

Guide to the Methods of Technology Appraisal, June 2008

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Assessment of cost-effectiveness

Main Challenges

- Specifying the comparator
- Measuring health benefits
- Sub-groups
- Uncertainty

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Specifying the comparator

- The comparator for the technology being assessed is very important because the choice to a large extent determines the incremental costs and incremental effects (and thus the cost per QALY).
- Relevant comparators might include:
  - Therapies routinely used in the NHS
  - Current best practice
  - Best supportive care
  - What is expected to be replaced (SMC)
- Blended comparators

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Febuxostat in the management of hyperuricaemia in people with gout

- High concentration of uric acid leads to crystals forming and these cause inflammation and pain, and if untreated can cause significant tissue damage.
- The company chose fixed dose (300 mg) allopurinol as the comparator arguing that this was the therapy routinely used in the NHS
- However, expert clinical opinion was firmly of the view that current best practice was to start at 300 mg & up-titrate to 900 mg (if necessary & if tolerated)
- This reduces the incremental benefits markedly without reducing the incremental cost much (since febuxostat costs 13 times as much as allopurinol)

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Pulmonary Arterial Hypertension

	Cost per QALY (versus best supportive care) in patients in NYHA functional class III	
Treatment assumed in NYHA class IV	IV epoprostenol	best supportive care
bosentan	27K	42K
sitaxentan	25K	44K
sildenafil	dominant	9K

IV epoprostenol 343K per QALY in NYHA functional class IV

Appraisal Consultation Document February 2008

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Romiplostim for treatment of chronic idiopathic thrombocytopenic purpura

- Agreed that comparison should be **Romiplostim + standard care vs. standard care** but what is standard care?
- Manufacture took the view that it was “watch and rescue” (involving substantial costs in terms if IV immunoglobulin)
- Appraisal Committee rejected this “because the population for whom romiplostim holds a marketing authorisation would be those for whom active treatment would be offered under current UK practice”
- Assuming comparator was active treatment with rituximab increased the ICERs substantially

ACD November 2009

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Measurement of Health Benefit

- The incremental QALYs as a result of a treatment have two components:
  - Changes in survival
  - Changes in health-related quality of life
- The main challenge with estimating changes in survival arises because the data on clinical effectiveness typically requires long-term survival to be extrapolated from short-term data
- Two challenges recur with quality of life data: (1) the absence of data; (2) unsatisfactory measure of quality of life

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Extrapolating survival

- "The vast majority of technology appraisals have not taken a systematic approach to survival analysis … the extent to which chosen methods have been justified differs markedly"
- Choice of function matters. Sunitinib for renal carcinoma

Model	Mean survival (IFN)	Mean survival (sunitinib)	Mean survival gain
Weibull	93.9	130.6	36.8
Exponential	144.2	217.3	73.1
Gompertz	78.3	98.2	19.9
Log-logistic	220.6	305.2	84.6

Latimer, N. *NICE DSU Technical Support Document 14*

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Azacitadine for myelodysplastic syndromes

- No preference-based measures collected in the AZA trials
- For AZA & best supportive care patients health state values generated by **mapping from QLQ-30 to EQ-5D** using algorithm developed from 199 patients with inoperable esophageal cancer
- For standard dose & low dose chemotherapy patients health state values generated by **mapping from SF-12 to SF-6D** using an algorithm developed from representative sample of 611 members of the UK general population (applied to data from 43 AML/MDS patients)
- Health state value for Acute Myeloid Leukaemia **assumed** to be 0.67

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Identifying sub-groups

- Cost-effectiveness generally varies across sub-groups
- Important because ICER for entire patient group may be above the threshold **but** there may be sub-groups for whom the intervention is cost-effective
- Similarly an ICER below the threshold for the patient group as a whole may hide ICERs for particular sub-groups **above** the cost-effectiveness threshold
- RCTs often under-powered to assess treatment effects in sub-groups. Doesn't imply that we cannot estimate cost-effectiveness by sub-group – simply increases uncertainty.

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Uncertainty

- Many sources of uncertainty two of the most important of which are parameter uncertainty & structural uncertainty
- There is uncertainty concerning the true value of most of the parameters in an economic model. As a consequence there is uncertainty regarding the ICER
- Important that any evaluation attempts to capture the extent of uncertainty & its implication for the interpretation of the base case ICER
- The two main weaknesses apparent in the treatment of uncertainty are:
  - exploring uncertainty in too few parameters
  - failing to justify range of values considered
- Structural uncertainty not generally explored much

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Uncertainty

- Probabilistic sensitivity analysis is preferred
  - Enables uncertainty associated with parameters to be simultaneously reflected
  - Provides the best estimates of mean costs and outcomes

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Developments

- **Appraising life-extending, end of life treatments**
- **Patient Access Schemes**
- **Value-based pricing**
- **Methods review 2012**

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Appraising life-extending, end of life treatments

- Introduced 5 January 2009, revised July 2009
- Three criteria in order to qualify:
  - The treatment is indicated for patients with a short life expectancy, normally < 24 months
  - There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared to current NHS treatment
  - The treatment is licensed or otherwise indicated for small patient populations
- Decisions to date imply £50,000 per QALY threshold

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Patient Access Schemes

- Voluntary agreement between Department of Health and the Association of the British Pharmaceutical Industry. Pharmaceutical Price Regulation Scheme 2009
- Target return on capital
- Encouragement of Patient Access Schemes
- E.g. cetuximab for colorectal cancer manufacturer rebates 16% of amount of cetuximab used; trabectedin for soft tissue sarcoma the cost is met by manufacturer after 5th cycle of treatment
- More recently: straight confidential price discount agreed with the DH e.g. Azacitidine for myelodysplastic syndromes; and Romiplostim for chronic idiopathic thrombocytopenic purpura

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Value-Based Pricing

- Consultation document Dec 2010
- Basic cost-effectiveness threshold reflecting health gains displaced when new treatments are funded
- Higher thresholds where greater “burden of disease”
- Higher thresholds for medicines demonstrating greater therapeutic innovation and improvement
- Higher thresholds for medicines displaying wider societal benefits

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Value-Based Pricing

- Summarising the comments received government noted "***that the responses are generally consistent with the possible approach proposed in the consultation, whereby the Burden of Illness of a condition is defined as the health loss currently suffered by patients, and Therapeutic Innovation and Improvement is measured on the basis of the quantity of health gain provided by a treatment"***
- Haven't indicated how VBP will be done (or by whom). Due to be introduced in Jan 2014.
- Emphasis on calculating weighted QALYs and then calculating a maximum price at which the medicine would be cost-effective

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Review of methods

- Methods of Technology Appraisal are subject to review and are evolving
- E.g. July 2011 while evaluating Mifamurtide for osteosarcoma in children, adolescents and young adults
- ***Where the Appraisal Committee has considered it appropriate to undertake sensitivity analysis on the effects of discounting because treatment effects are both substantial in restoring health and sustained over a very long period (normally at least 30 years), the Committee should apply a rate of 1.5% for health effects and 3.5% for costs***

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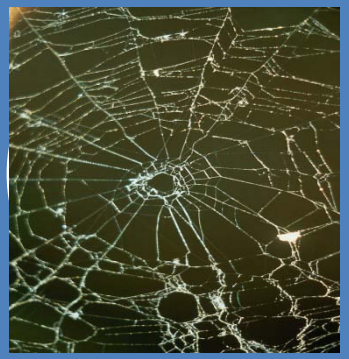
Many challenges remain

National versus local decision-making



Time taken to produce guidance

Legitimacy (e.g. cost per QALY threshold)

Marketing for Pharma

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