NICE Guidelines for HTA – Issues of Controversy

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Outline

• (Brief) policy context
• Variation in methods guidance between jurisdictions
• Controversial areas of methods guidance (at NICE)
  – Perspective
  – Measuring benefits
  – Dealing with uncertainty in decision making
  – Use of indirect comparison
  – Modelling methods
  – Heterogeneity and sub-groups
Policy context

**Spectrum of requirements in centralised reimbursement**

Focus on clinical evidence  
Some budget impact  
Focus on trial comparators

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Focus on value/CE  
Long-term modelling  
Full range of comparators

France  
Germany  
Managed care US  

Australia  
Canada  
UK

Plan for ‘sophisticated’ end of spectrum and adapt as necessary
### Variability in methods guidelines

#### Choice of comparator (n=27)

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most commonly used</td>
<td>8</td>
</tr>
<tr>
<td>Existing, most effective or minimum practice</td>
<td>2</td>
</tr>
<tr>
<td>Existing or most effective</td>
<td>1</td>
</tr>
<tr>
<td>Justify</td>
<td>1</td>
</tr>
<tr>
<td>Existing and no treatment</td>
<td>2</td>
</tr>
<tr>
<td>Most common, least costly, no treatment</td>
<td>1</td>
</tr>
<tr>
<td>Most common, least costly, no treatment, most effective</td>
<td>2</td>
</tr>
<tr>
<td>Most common, least costly, most effective</td>
<td>1</td>
</tr>
<tr>
<td>Most likely to be displaced</td>
<td>1</td>
</tr>
<tr>
<td>Most efficient, most effective, do nothing</td>
<td>2</td>
</tr>
<tr>
<td>All relevant comparators</td>
<td>2</td>
</tr>
<tr>
<td>Most effective and no treatment</td>
<td>1</td>
</tr>
<tr>
<td>Not clear/specific</td>
<td>3</td>
</tr>
</tbody>
</table>

## Variability in methods guidelines

### Methods for sensitivity analysis (n=27)

<table>
<thead>
<tr>
<th>Method Description</th>
<th>Count</th>
</tr>
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<tbody>
<tr>
<td>Need to state and justify</td>
<td>3</td>
</tr>
<tr>
<td>Not stated/not specific</td>
<td>10</td>
</tr>
<tr>
<td>Probabilistic sensitivity analysis (PSA)</td>
<td>3</td>
</tr>
<tr>
<td>One-way, multi-way</td>
<td>1</td>
</tr>
<tr>
<td>One-way, two-way</td>
<td>2</td>
</tr>
<tr>
<td>Multi-way (of most important)</td>
<td>1</td>
</tr>
<tr>
<td>One-way, multi-way and PSA</td>
<td>5</td>
</tr>
<tr>
<td>One-way, multi-way and worst-best scenario</td>
<td>1</td>
</tr>
<tr>
<td>One-way with tornado diagram</td>
<td>1</td>
</tr>
</tbody>
</table>

Implications of analysts

Which type of analyst?

Seeking to inform multiple specific decision-makers

- The same analysis will not inform all decision makers
- Multiple analyses necessary
- Need for analytic flexibility
- For primary data collection: specification of patients, locations and data capture

Seeking to inform single specific makers

- Need to be specific about decision maker
- Still a potential need for multiple analyses
- Primary data collection: representativeness of sample

Sculpher MJ, Drummond MF. *Pharmacoeconomics* 2006;11:1087-1099.
Implications for decision makers

The problem of variable methods guidelines

<table>
<thead>
<tr>
<th>Variation legitimate</th>
<th>Variation expected</th>
<th>Variation inappropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.g. Perspective, objective function, comparators, parameter estimates</td>
<td>E.g. Descriptive system for health, source of preference values</td>
<td>E.g. Need to use all evidence, consistent perspective, generic measure of health</td>
</tr>
</tbody>
</table>

Define and justify

Define and justify

National and international reference cases

Education and training

Sculpher MJ, Drummond MF. *Pharmacoeconomics* 2006;11:1087-1099.
Areas of controversy at NICE

- Perspective
- Measuring health benefits
- Dealing with uncertainty in decision making
Perspective

2008 methods guidance

“Some technologies may have a substantial impact on the costs (or cost savings) to other government bodies. In these exceptional circumstances, costs to other government bodies may be included if this has been specifically agreed with the Department of Health, usually before referral of the topic. When non-reference-case analyses include these broader costs, explicit methods of valuation are required. In all cases, these costs should be reported separately from NHS/PSS costs. These costs should not be combined into an incremental cost-effectiveness ratio (ICER; where the QALY is the outcome measure of interest).

Cost-effectiveness at NICE

Price > $P^*$ $60,000
Price = $P^*$ $40,000
Price < $P^*$ $20,000

Net Health Benefit
1 QALY

Problems with widening the perspective

- NICE’s perspective defined by its responsibilities
- NICE effectively ignores wider costs because of budget constraint
  - Non-NHS public sector
  - Patients
  - Productivity
- Wider perspective have major implications
  - Opportunity costs other than health
  - Health budget used to fund non-health outcomes
  - Current CEA framework not adequate
- Alternative: a meta decision maker
  - All sectors work like NHS (through NICE)
  - Provide budget adjustments over time
Measuring health benefits

What should the health metric look like?

• Need to be generic
  – Decisions across diseases and clinical specialties
  – Need to be able to compare health gain with health opportunity costs

• Unclear role for disease-specific measures of health
  – Unless ring-fenced budgets
  – No effects of technologies outside the disease of interest

• Needs to combine key dimensions of health
  – Length of life
  – Health-related quality of life

• NICE’s requirement – health quantified in terms of QALYs
Why the QALY as a generic measure of individual health?

- Some empirical work to suggest QALYs imperfectly reflect individual preferences
- Little empirical work in the context of HTA informing real decisions
- Alternative measures developed but rarely applied (e.g. healthy-year equivalent)
- QALY legitimate to inform decisions
  - Widely used in empirical studies
  - Is (or should be) transparent
  - Strengths and weaknesses understood
  - Experience in alternative formal measures limited
  - Further research essential
Interpersonal comparisons of health gain

“A QALY is a QALY is a QALY”

- Severity of baseline prognosis
- Lifetime health experience
- Non health-related disadvantage
- End of life
- Degree of ‘blame’

Those that gain health:
Generally known

Those that lose health:
Generally unknown
Inter-personal comparison of health
The analytic approach

• Concept of an ‘equity weighted’ QALY or a measure of the social value of health
• Literature exists
  – Methods of elicitation
  – Surveys of public preferences
  – Methods to augment/replace QALYs
• Limited use in applied studies
• What characteristics of individuals should be taken into account and who should select these?
• How should these characteristics be weighted/valued and by whom?
Inter-personal comparison of health
The deliberative approach approach

• Unweighted QALY gains in analysis do not mean these remain unweighted in decision making
• Range of factors which could be taken into account other than ICER versus
  – Inadequacy of QALY
  – Characteristics of gainers and losers
  – Innovative nature of the product
  – Sufficiency of evidence
NICE’s ‘end of life’ guidelines

Details of guidelines at end of life

• In contexts where benefits are not adequately captured in Reference Case and ICER>£30,000

• Specific (key) criteria:
  – Life expectancy less than 24 months
  – Good evidence that treatment extends life by at least 3 months

• Further analysis:
  – Is the treatment cost-effective when terminal stage of disease valued as good health?
  – What additional weight needs to be given to the QALY gained to make it cost-effective?

• Follow-up data collection likely

• Relates to small populations
Dealing with uncertainty in decisions

The context

Launch

Regulatory trials
- comparators?
- which patients?
Limited head-to-head
Some safety

Market access

Phase IV
- comparative?
- randomised?

Routine use

Knowledge about use
Safety data increases

Limited evidence
Potential for more evidence
Limits to gaining more evidence
## Uncertainty matters

### The evidence

<table>
<thead>
<tr>
<th></th>
<th>95% CI</th>
<th>Mean</th>
<th>95% CI</th>
</tr>
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<tr>
<td>Risk of MI or CV death</td>
<td>2%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Treatment effect</td>
<td>0.7</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Cost of MI</td>
<td>£4K</td>
<td>£6K</td>
<td>£8K</td>
</tr>
<tr>
<td>HRQoL after MI</td>
<td>0.4</td>
<td>0.6</td>
<td>0.8</td>
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<td>Mortality risk after MI</td>
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Based on ‘mean’ estimates:
Cost per QALY gained < £20,000

Allowing for uncertainty:
0.4 chance >£20,000

Uncertainty imposes costs:
The wrong decision leads to loss in QALYs

Need to balance the cost of research against its value in reducing the cost of uncertainty
Making decisions under uncertainty
A two-decision world

- Costs of research are too high compared to reduction in cost of uncertainty
- ‘External’ research is underway and the costs of reversing the decision modest
- Further research will not be disincentivised
- No more research is feasible

- Research of value: costs of research are low compared to reduction in cost of uncertainty
- High costs of reversing a decision following research
- ‘Yes’ decision likely to disincentivise research

Positive guidance

Negative guidance
# Making decisions under uncertainty

## More nuanced decisions

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<th>Arrangement</th>
<th>Considerations</th>
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<tr>
<td>Only in research</td>
<td>• How different from a ‘no’ decision?</td>
</tr>
<tr>
<td></td>
<td>• Cost per QALY&lt;$20,000</td>
</tr>
<tr>
<td></td>
<td>• Clear justification</td>
</tr>
<tr>
<td></td>
<td>• Define what research is needed</td>
</tr>
<tr>
<td>Patient access schemes</td>
<td>• Reduce effective price of product</td>
</tr>
<tr>
<td></td>
<td>• Lowers cost per QALY</td>
</tr>
<tr>
<td></td>
<td>• Can reduce the cost of uncertainty</td>
</tr>
<tr>
<td>Conditional guidance</td>
<td>• Define what research is needed</td>
</tr>
<tr>
<td></td>
<td>• Will research be undertaken by manufacturer?</td>
</tr>
<tr>
<td></td>
<td>• What cost to the NHS?</td>
</tr>
<tr>
<td></td>
<td>• Cost of reversing the decision</td>
</tr>
<tr>
<td>Conditional guidance</td>
<td>• How is effective price lowered?</td>
</tr>
<tr>
<td>(at lower effective price)</td>
<td>• Can incentivise research (get premium price)</td>
</tr>
<tr>
<td></td>
<td>• Cost of NHS undertaking the research</td>
</tr>
<tr>
<td></td>
<td>• Cost of reversing the decision</td>
</tr>
</tbody>
</table>
Thanks…

http://www.york.ac.uk/inst/che/staff/sculpher.htm

Centre for Health Economics’ short courses:  
http://www.york.ac.uk/inst/che/training/index.htm#short