What is the “Right” Cost Per QALY for Innovative and Life Saving Oncology or End-of-Life Therapies

Educational Symposium sponsored by Pfizer
ISPOR 4th Asia-Pacific Conference
5 September 2010 Phuket, Thailand

Objectives of Educational Symposium

- This symposium will explore the rational and practical implication of NICE revised guideline
- To discuss what is the “right” cost effectiveness criteria for technology adaptation and should there be a higher threshold for cancer drugs, biological, and other end of life care therapies

Assessing Cost Effectiveness

<table>
<thead>
<tr>
<th>Cost per QALY (£'000)</th>
<th>Probability of rejection</th>
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<tr>
<td>10</td>
<td>High</td>
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<tr>
<td>20</td>
<td>High</td>
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<td>30</td>
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<tr>
<td>40</td>
<td>Low</td>
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<tr>
<td>50</td>
<td>Low</td>
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Rituximab for follicular lymphoma
Imatinib (Glivec) for chronic myeloid leukaemia
Trastuzumab (Herceptin) for early stage HER-2 positive breast cancer

Measuring the QALY of Life
Professor: Richard argues that the key measure of health spending effectiveness is quality-adjusted life years (QALY). In this exhibit, he shows a line showing the trade-offs between the cost of treatments and their QALY payoff. As the curve slopes, that trade-off becomes less and less attractive.

What is the view of NICE?

- NICE has not raised the value of its cost per QALY threshold since it first made public
- The opportunity cost could be increased based on the inflation, health budget, small patient population, different locality and the extension of life expectancy
- NICE has introduced new criteria in 2009 and increased the threshold for end of life treatments based on the willingness-to-pay

The Center Topics of the Symposium

- What is the right threshold for the HTA evaluation?
- Does different disease require different threshold or more consideration should be given beyond the threshold?
- What is the global experience of the threshold application?
Symposium Agenda

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Speaker &amp; Affiliation</th>
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<tr>
<td>6:30 pm</td>
<td>Introduction</td>
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<td></td>
<td>Prof. Shanlian Hu</td>
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<td>Fudan University, Shanghai, China</td>
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<tr>
<td>6:35 pm</td>
<td>NICE end-of-life guideline and its implications</td>
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<td>Prof. Kenneth KC Lee</td>
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<td>BSc, MPhil, PhD. Head of Pharmacy School of Med. &amp; Health Sci. Monash Univ., Sunway Campus. Adjunct Prof. School of Pharmacy CUHK</td>
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<tr>
<td>6:55 pm</td>
<td>Global Experience on ICER Criteria Application</td>
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<td>Dr. Boxiong Tang MD, PhD. Sr. Director Outcomes Research, Emerging Markets Pfizer, Inc.</td>
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<tr>
<td>7:15 pm - 7:30 pm</td>
<td>Q &amp; A, Open discussion and conclusion</td>
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<td></td>
<td>All speakers</td>
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Outline of Presentation

- Background
- NICE guideline on end-of-life (EOL) care
- Implications
- Summary

General background

- NICE was established in 1999 under the Labour Party
- NICE is responsible for assessing the effectiveness and cost-effectiveness of treatments, and making recommendations to the UK NHS based on the best evidence available
- Threshold value set at £30,000/QALY gained as the upper limit, but the range of £20,000 - £30,000 has been used for a number of years
- Research showed an increasing likelihood of rejection as the ICER exceeded £15,000 (Rawlinns and Culyer 2004)
- In recent years, increasing circumstances in which it may be appropriate to recommend treatments with higher incremental cost effectiveness ratios
- NICE (2009): ‘Above a most plausible ICER of £30,000 per QALY gained, the Appraisal Committee will need to identify an increasingly stronger case for supporting the technology as an effective use of NHS resources.’
- Appraisal Committees have previously made recommendations above the normal threshold range when they have explicitly identified additional benefits in new health technologies

NICE End-of-Life Guideline and its Implications

Kenneth KC Lee
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Professor of Pharmacy and Head of Pharmacy School of Medicine and Health Sciences Monash University, Sunway Campus, Malaysia
Visiting Professor University of London School of Pharmacy
Adjunct Professor School of Pharmacy CUHK
Adjunct Professor Faculty of Medicine HKU

Cost-effectiveness methods at NICE
NICE’s conception of value

From: McCabe et al 2008
Background of NICE EOL Policy

- In 2008, an Appraisal Committee led by Coon and 6 other health economists was appointed by NICE to appraise on bevacizumab, sorafenib, sunitinib, and temsirolimus for renal cell carcinoma.
- The team found that the new drugs were clinically better than existing treatments in a number of patient groups and disease scenarios.
- In terms of cost/QALY, it was found that none of the 4 drugs came even close if £30,000 was used as the threshold; in addition, in comparing 2 of the drugs, an extra £31,185 only extends patient’s life by 5 months.
- Conclusion: evidence was not clear-cut.
- Result was subsequently endorsed by NICE who immediately became the target of intense organized lobbying from stakeholders.
- Intense criticism from press and politicians.

NICE Supplementary Advice on EOL (2009)


This supplementary advice is applied in the following circumstances and when all the criteria referred to below are satisfied:

- for patients with a short life expectancy, normally less than 24 months and;
- 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, and;
- is licensed or otherwise indicated, for small patient populations.

When the conditions described above are met, the Appraisal Committee will consider:

- The impact of giving greater weight to QALYs achieved in the later stages of terminal diseases, using the assumption that the extended survival period is experienced at the full quality of life anticipated for a healthy individual of the same age, and;

- The magnitude of the additional weight that would need to be assigned to the QALY benefits in this patient group for the cost-effectiveness of the technology to fall within the current threshold range.

NICE’s Views

- In developing this supplementary advice, the Appraisal Committees’ previous decisions, together with the relevant principles of Social Value Judgements have been taken into account.
- The change reflects the beliefs and desires of the British public and it has also responded to scientific and public concern.
- Regard has been given to the circumstances in which it might be appropriate to support the use of treatments outside its cost per QALY threshold range.
- NICE’s responsibility to recognise the potential for long term benefits to the NHS of new innovation products.
- Objectives of NICE Supplementary Advice: “The objective of the supplementary advice was to ensure that the Appraisal Committees fully consider all the benefits which it is appropriate to take into account in appraising treatments designed to extend life, at the end of life, for small populations and in particular to ensure that where benefits are not, or not adequately captured in the reference case, that the Appraisal Committees are provided with an appropriate supplementary analysis.”

Controversies and Arguments

- NICE is not to decide on health budget by setting a fixed threshold but to maximize the health gains from a fixed budget.
- NICE threshold: opportunity cost of accepting a technology i.e. health gain foregone by other patients.
- Equity issue: should all patients be assumed the same in considering health gains or losses?
- Concerns arising from politicians and influence by media.

Implications

- Treatments that may have been previously ruled out as not sufficiently cost effective for routine use in the NHS might now be recommended for use.
- Treatments that are licensed for small patient populations and that will increase a short life expectancy by at least 3 months will be considered.
- NICE will support the development of novel treatments for smaller patient groups that provide innovative benefits over and above existing NHS care.
- Appraisal Committees will consider the impact of giving greater weight to extensions to life when people have a short remaining life span.
- Interventions with a large budgetary impact may be appraised using a lower threshold due to opportunity cost and equity consideration.
- The value reflected in the currently adopted threshold may need to be reviewed regularly to reflect the impact of changes and budget over time.
- New technologies will be assessed individually based on their merits compared to existing ones.
The Everolimus case

- An estimated eight week cycle of treatment would cost £5,264 per patient
- Estimated Cost/QALY gained is almost double what NICE would normally allow
- Sir Andrew Dillon: “A diagnosis of renal cancer is devastating for patients and those who care for them and we are disappointed not to be able to recommend everolimus as a second line treatment option. However, we too have to ensure that the money available to the NHS is used to best effect, particularly when NHS funds, like the rest of the public sector, is under considerable financial pressure.”

Equity issue

- 2 groups of patients affected: those who receive new treatments and those who bear the opportunity cost
- An assumption inherently made in making a recommendation: the health gain foregone by those who bear the opportunity cost (typically elderly and in the last year of life) is valued less than that of those who receive the new treatment
- Theoretically, to ensure equity, the patients who did eventually bear the opportunity cost need to be identified for characteristics analysis, but this is realistically not achievable → broad generalizations are often made instead of specific identification of patients whose health gains are displaced
- Is there any ground for ensuring equity in health gains and losses of different categories of patients?

A moving threshold

Not deemed desirable:
- Threshold only provides a means for optimum allocation of a fixed budget, but not necessarily representing the society’s willingness to pay for health
- Introduce uncertainty and provide less secure environment for innovation
- May encourage unnecessary high risk investment in developing new technologies

(McCabe, Claxton and Culyer 2008)

Summary of messages

- Final outcome of NICE appraisal process is influenced by many social, economic and political factors
- NICE sees itself not to determine the health budget for UK by setting an independent threshold, but to ensure the maximum health gain from a fixed budget
- NICE threshold is best to be fixed to avoid uncertainties for parties concerned
- Although assumptions are inevitably made in recommending new technologies, opportunity cost consideration is important to achieve optimum weighting of the health gains/losses between different patient groups

Global Experience on ICER Criteria Application

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ISPOR 4th Asia-Pacific Conference
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Outline of Presentation

- Background on UK/Canada appraisals on end-of-life (EOL) care
- Sutent (Sunitinib) experiences
- Discussion and summary

NICE guidance on ICER

- Towse (2002) has suggested that the ‘threshold’ cost per quality adjusted life year gained implicit in NICE’s decisions is between £20,000 and £30,000; technologies with incremental cost-effectiveness ratios above this level seem more likely, but not certain, to be rejected

Towse A. What is NICE’s threshold? An external view. Chapter 1 in: Cost effectiveness thresholds: economic and ethical issues. 2002

NICE appraisals on end-of-life (EOL) care

NICE technology appraisals of cancer drugs - 1999 to 2008

<table>
<thead>
<tr>
<th>Total # cancer drug appraised</th>
<th>42</th>
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<tbody>
<tr>
<td>Recommended or minor restriction</td>
<td>22</td>
</tr>
<tr>
<td>Major restriction</td>
<td>13</td>
</tr>
<tr>
<td>Not recommended</td>
<td>7</td>
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NICE historically had a track record of approving more oncology medications at the upper bound of acceptability than non-oncology medications; however, more recently there has been a rejection of multiple drugs for advanced cancer

NICE New Guidance

- In January 2009, NICE adopted new guidance for EOL drug appraisal:
  - Small patient population
  - Short life expectancy (normally less than two years)
  - Extension of life expectancy (normally at least three months)
  - No alternative treatment with comparable benefits available through the NHS

Sunitinib malate (SUTENT)

- Sunitinib malate (SUTENT) is a multi-kinase inhibitor, used to treat advanced metastatic renal cell carcinoma (MRCC) and gastrointestinal stromal tumor (GIST).
  - GIST (gastrointestinal stromal tumor)
    - a rare cancer of the stomach, bowel, or esophagus.
    - Treatment: surgery & Gleevec® (imatinib mesylate)
Metastatic renal cell carcinoma (MRCC)

- Kidney cancer is a rare disease (4400 new cases in Canada in 2008, 1600 deaths)
- 80 - 85% were RCC & is most aggressive type
- 25% of patients with metastases at diagnosis & 50% will develop to advanced
- Prognosis of MRCC was extremely poor (median OS is 6–12 months). Hormonal, chemo, and radiation therapy failed to significantly improve clinical outcomes
- IFN-a or IL-2 were used before the targeted therapy era, despite an overall remission of only 12.4%

Canadian Cancer Society. Canadian Cancer Statistics 2008

Sunitinib in MRCC - NICE recommendation

- In February 2009, NICE recommended sunitinib as 1st line treatment for patients with advanced MRCC who are suitable for immunotherapy and have an ECOG performance status of 0 or 1
- The latest NICE appraisal of sunitinib took into account the new evaluation criteria that factor in the added value society puts on life-extending treatments at the end of life. This could demonstrate that a broad perspective, which goes beyond the application of an ICER threshold, is used when evaluating drugs for advanced cancer or simply that a higher ICER threshold may be applied in this context

Case discussion: Sunitinib in Canada

How Do Cost Effectiveness Analyses Inform Reimbursement Decisions for Oncology Medications in Canada? The Example of Sunitinib for First-Line Treatment of Metastatic Renal Cell Carcinoma

Drug Indication ICER ($) Recommendation
Sorafenib Second-line MRCC 36K/LYG Do not list
Sunitinib Second-line MRCC 56K/QALY Do not list
Sunitinib Gastrointestinal stromal tumor 80K/QALY List (with criteria)
Sunitinib First-line MRCC 144K/QALY List (with criteria)

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Sunitinib Experience – 2nd line

- In August 2006, based on 2 single aim phase II trials, sunitinib was granted conditional approval in Canada for the 2nd line treatment of MRCC
- In April 2007, Common Drug Review (CDR), provided a “do not reimburse” recommendation for 2nd line use
- lack of RCT data in patients failed cytokine therapy
- uncertainty in both the survival benefit and the cost-effectiveness of sunitinib

CEDAC final recommendation on reconsideration and reasons for recommendation – Sunitinib renal

Sunitinib Experience – 1st line

- Phase III trial shown superior clinical benefits compared to IFN-a
- PF survival (11 m vs. 5 m),
- Objective response rate (31% vs. 6%),
- QoL (P < 0.001)
- Acceptable and manageable toxicity
- Health Canada revised the label to “for the treatment of MRCC of clear cell histology” with no further specification
- Joint Oncology Drug Review (JODR) committee concluded that 1st-line therapy with sunitinib appeared to be more effective and better tolerated than IFNa, but was not cost-effective


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Sunitinib experience – current reimbursement status

- Now, all provinces reimburse sunitinib for 1st-line therapy of MRCC and several provinces also fund it for second-line

- Treatment Guideline: Sunitinib is the 1st-line SOC for most patients with MRCC

Discussions

- Cost-effectiveness should be a criterion in the decision making process, but ICER is not the only criteria used in technology adoption
  - A higher ICER not necessary means automatic rejection

- Multiple factors are involved in the decisions to adopt a new technology
  - Canadian reimbursement decisions makers stated: “Anyone who has ever been involved in drug reimbursement decision-making knows that many factors in addition to the cost-effectiveness ratio affect the ultimate decision”

Factors may influence reimbursement decision

- Available resources
- Drugs for rare diseases
- Drugs that increase survival, & other clinical benefit
- Willingness to pay
- Budget impact (cost to government)
- Cost-effectiveness (ICER)
- Life-threatening condition (cancer drugs are more likely get positive recommendation)

Conclusions

- ICER is not necessary the only one criteria used in technology adoption

- Other benefits to patients should be thoroughly examined before reach the decision

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Question & Answer

Thanks