Budget impact vs cost effectiveness: Implications for personalised cancer therapies.

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no conflict of interest
The aim of the healthcare policy is to *maximise the health* of the population within the *limits of the available means* and within an ethical framework, based on values such as fairness and solidarity.
\[
\text{cost per life year gained (LYG)} = \text{incremental cost-effectiveness ratio}
\]
\[
\text{cost per quality-adjusted life year (QALY)} = \text{incremental cost-utility ratio}
\]
**ICER**

$\text{cost} / (\text{quality adjusted}) \text{ life year}$

- **cost**
  - less effective less costly
  - more effective less costly

- **effectiveness**
  - less effective more costly
  - more effective more costly

The diagram illustrates the relationship between cost and effectiveness, with ICER indicating the potential for treatments to be more or less effective and more or less costly.
<table>
<thead>
<tr>
<th>Country</th>
<th>Authors</th>
<th>ICER threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Explicit ICER threshold range</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>NICE&lt;sup&gt;151&lt;/sup&gt;</td>
<td>£20 000 - £30 000 per QALY</td>
</tr>
<tr>
<td><strong>Implicit ICER threshold values or ranges based on past allocation decisions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>Henry et al. and the PBAC&lt;sup&gt;95&lt;/sup&gt;</td>
<td>AU$69 900 per QALY</td>
</tr>
<tr>
<td>New Zealand</td>
<td>Pritchard et al. and PHARMAC&lt;sup&gt;93&lt;/sup&gt;</td>
<td>NZ$20 000 per QALY</td>
</tr>
</tbody>
</table>
| Canada           | Rocchi et al. and the CDR<sup>94</sup>  | Range of acceptance: dominant to CAN$80 000 per QALY  
Range of rejection: CAN$31 000 to CAN$137 000 per QALY |
| **ICER threshold values or ranges proposed by individuals or institutions** |                                         |                                                                                   |
| USA              | Weinstein<sup>140</sup>                 | $50 000 per QALY                                                                  |
| USA              | Braithwaite et al.<sup>96</sup>         | $109 000 - $297 000 per QALY                                                      |
| The Netherlands   | The Council for Public Health and Health Care<sup>156</sup> | €80 000 per QALY                                                                 |
| Canada           | Laupacis et al. 155                     | CAN$20 000 to CAN$100 000 per QALY                                                |
| **No ICER threshold values or ranges identified**                         |                                         |                                                                                   |
| Finland, Sweden, Norway, Denmark                                          |                                         |                                                                                   |

< 1*GDP / capita = cost-effective  
> 3*GDP / capita = cost-ineffective

Cleemput et al, report 100 KCE, 2009
cost-effectiveness trastuzumab *in early stage breast cancer*
cost-effectiveness trastuzumab in early stage breast cancer

ICER: 34,999€ / 16,026€ / 5,994€

4,160€ - 64,322€

Huybrechts et al, report 34 KCE, 2006
cost-effectiveness trastuzumab in early stage breast cancer

Huybrechts et al, report 34 KCE, 2006
Cost per test € 300
Incr. cost per treatment € 25000
True positive treated gains 1 QALY
False positive treated loses 0.1 QALY

ICER (€/QALY)
Specificity of test for target population

5% target
20% target

Personal communication F. Hulstaert
acceptable... and affordable?
health care spending as percent of GDP

Source: OECD
“How much will Herceptin really cost?”

“On the face of it, the answer to our question is simple—Herceptin will cost our trust £2.3m, but the real cost lies in the services that will be cut to provide this money.”

Table 1 Cost and potential benefits of adjuvant cancer treatments in Norfolk and Norwich University Hospital Trust

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No of patients given treatment</th>
<th>Drug cost (£000)</th>
<th>Proven benefit</th>
<th>Potential benefit at our hospital</th>
<th>Cost per patient cured (£000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant chemotherapy for lung cancer</td>
<td>15</td>
<td>23</td>
<td>5-15% improved 5 year overall survival&lt;sup&gt;mg3&lt;/sup&gt;</td>
<td>1 extra patient cured</td>
<td>23</td>
</tr>
<tr>
<td>Oxaliplatin as adjuvant therapy for colon cancer compared with fluorouracil alone</td>
<td>20</td>
<td>137</td>
<td>5% improved 3 year disease-free survival; no benefit to overall survival&lt;sup&gt;mg4&lt;/sup&gt;</td>
<td>1 extra patient without recurrence at 3 years</td>
<td>137</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy for oesophageal cancer</td>
<td>25</td>
<td>8</td>
<td>9% improved 5 year survival&lt;sup&gt;mg5&lt;/sup&gt;</td>
<td>3 extra patients cured</td>
<td>2.67</td>
</tr>
<tr>
<td>Rituximab in addition to CHOP for non-Hodgkin lymphoma in patients over 60</td>
<td>25</td>
<td>215</td>
<td>13% improved 2 year overall survival&lt;sup&gt;mg6&lt;/sup&gt;</td>
<td>3 extra patients cured</td>
<td>71.67</td>
</tr>
<tr>
<td>Adjuvant aromatase inhibitors in postmenopausal breast cancer</td>
<td>270</td>
<td>120</td>
<td>3.7% improved disease-free survival compared with tamoxifen; no benefit to overall survival&lt;sup&gt;mg7&lt;/sup&gt;</td>
<td>8 extra patients without recurrence at 5 years</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>355</td>
<td>503</td>
<td>16 extra patients cured</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herceptin for early stage breast cancer</td>
<td>75</td>
<td>1940</td>
<td>0-4% improved 4 year overall survival&lt;sup&gt;w1 w2&lt;/sup&gt;</td>
<td>3 extra patients cured</td>
<td>650</td>
</tr>
</tbody>
</table>

Ann Barrett et al, BMJ 2008
acceptability vs. affordability

There is growing recognition that a comprehensive economic assessment of a new health-care intervention at the time of launch requires both a cost-effectiveness analysis (CEA) and a budget impact analysis (BIA).
<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>BIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research question</strong></td>
<td>Acceptability</td>
<td>Affordability</td>
</tr>
<tr>
<td><strong>Perspective</strong></td>
<td>Healthcare payers</td>
<td></td>
</tr>
<tr>
<td><strong>Target population</strong></td>
<td>Consistent with reimbursement request</td>
<td>Open</td>
</tr>
<tr>
<td></td>
<td>Closed *</td>
<td></td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>On the efficiency frontier</td>
<td>Current situation</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td>Direct healthcare related costs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No transfers</td>
<td>Transfers</td>
</tr>
<tr>
<td><strong>Health outcomes</strong></td>
<td>Included</td>
<td>Not included **</td>
</tr>
<tr>
<td></td>
<td>As long as incremental costs or outcomes are generated</td>
<td>Up to steady state</td>
</tr>
<tr>
<td><strong>Time horizon</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Modelling</strong></td>
<td>Decision tree, Markov model…</td>
<td></td>
</tr>
<tr>
<td><strong>Handling uncertainty</strong></td>
<td>Probabilistic and one- or multiple-way probabilistic sensitivity analyses, scenario and subgroup analyses</td>
<td></td>
</tr>
<tr>
<td><strong>Discount rate</strong></td>
<td>Costs: 3%, effects: 1.5%</td>
<td>No discounting</td>
</tr>
<tr>
<td><strong>Presenting results</strong></td>
<td>Incremental cost, incremental effect, ICER, cost-effectiveness plane, CEA-curve, results of the sensitivity analyses</td>
<td>Yearly budget impact, disaggregated impact, results of the sensitivity analyses</td>
</tr>
</tbody>
</table>

*C: Consistent

**: Not consistent

*Cleemput et al, Report 183 KCE, 2012*
<table>
<thead>
<tr>
<th>stage</th>
<th>FISH positive</th>
<th>Actual Chemo</th>
<th>Chemo LVEF ≥55%</th>
</tr>
</thead>
<tbody>
<tr>
<td>stage 1</td>
<td>378</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.25 M€</td>
</tr>
<tr>
<td>stage 2</td>
<td>546</td>
<td>331</td>
<td>267</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.86 M€</td>
</tr>
<tr>
<td>stage 3</td>
<td>245</td>
<td>179</td>
<td>144</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.85 M€</td>
</tr>
<tr>
<td>all</td>
<td>1169</td>
<td>610</td>
<td>491</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19.96 M€</td>
</tr>
</tbody>
</table>

Belgian population data, 2005

Adapted from Huybrecht et al, Report 34 KCE, 2006
some issues

many new drugs in the pipeline
rapidly evolving and highly complex landscape
smaller numbers of potential recipients
what is the evidence?
higher costs of newer drugs
what ICER benchmark to use?
allow different prices for different patient groups?
value-based pricing?
value-based user charges?
how to value?
how to deal the ever growing health care basket?
...
RCT’s: time for a paradigm change?

Which populations do really benefit?
  RCT’s in small and highly selected population?

The drug and its companion diagnostic
effectiveness? Value? Timing?

Longer survival versus less side-effects and better QOL
  New RCT’s without cross-over?

New approaches for trial design?
  Bayesian adaptive trials, modelling

How to meet the evidence needs of reimbursement authorities?
  Supplementary support by observational cohorts?
  Post-authorization data?
The diagram illustrates the lifecycle of technology development and adoption, highlighting key phases and decision points.

- **Preclinical & Safety**: Early-stage research and development to ensure safety and efficacy.
- **Emerging**: Technologies in Phase I-II-III clinical trials in selected centers.
- **Diffusing**: Technologies becoming more widespread, with CEA & BIA (Cost-Effectiveness Analysis & Benefit-Cost Analysis) evaluation.
- **Established**: Technologies are widely adopted, with reduced financing.
- **Obsolete**: Technologies become outdated or outmoded, requiring new innovations.

Key stages include:
- **Effectiveness**: Demonstrating the technology's benefits.
- **Pricing (Cost?)**: Evaluating financial aspects.
- **Financing**: The funding landscape as technology moves through different phases.

The diagram graphically shows the extent of clinical use over time (t), with arrows indicating milestones and decision points.
investment

- Premarket development
- Emerging: in silico studies, Phase I-II in selected centres
- Diffusing: RCT unethical? Widespread use still avoidable?
- Established
- Obsolete

Performance & safety
Effectiveness?
Cost calculation?
CEA - BIA
Financing
similar issues for radiotherapy

many new **technologies** in the pipeline
rapidly evolving and highly complex landscape
smaller numbers of potential recipients
what is the evidence?
higher costs of newer **technologies**
what ICER benchmark to use?
allow different prices for different patient groups?
value-based pricing?
value based user charges?
how to value?
how to deal the ever growing health care basket?
...

Reimbursement for SBRT?

What is the (level 1) evidence?
The cost?
The value for money?
The budgetary impact?
coverage with evidence development

- Innovative radiotherapy techniques
- Define the indications
- Define the costs to be covered
- Define the evidence generation
- Evidence generation and follow-up

In close collaboration with the radiotherapy departments
<table>
<thead>
<tr>
<th>Technique</th>
<th>Cancer Indication</th>
<th>Safety monitoring (clinical trial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APBI</td>
<td>Breast (low risk group only)</td>
<td>No**</td>
</tr>
<tr>
<td>APBI</td>
<td>Breast (medium risk)</td>
<td>Yes</td>
</tr>
<tr>
<td>Intraoperative boost</td>
<td>Breast</td>
<td>No**</td>
</tr>
<tr>
<td>SBRT</td>
<td>Lung</td>
<td>No</td>
</tr>
<tr>
<td>SBRT</td>
<td>Prostate</td>
<td>Yes</td>
</tr>
<tr>
<td>SBRT</td>
<td>Renal</td>
<td>Yes</td>
</tr>
<tr>
<td>SBRT</td>
<td>Pancreatic</td>
<td>Yes</td>
</tr>
<tr>
<td>SBRT</td>
<td>Head &amp; Neck</td>
<td>Yes</td>
</tr>
<tr>
<td>SBRT</td>
<td>Primary Hepatic</td>
<td>Yes</td>
</tr>
<tr>
<td>SBRT</td>
<td>Hepatic Metastases</td>
<td>No</td>
</tr>
<tr>
<td>SBRT</td>
<td>Spinal and paraspinal</td>
<td>No</td>
</tr>
<tr>
<td>SBRT</td>
<td>Oligometastases (other)</td>
<td>Yes</td>
</tr>
<tr>
<td>SBRT</td>
<td>Lung Metastases</td>
<td>No</td>
</tr>
<tr>
<td>SBRT</td>
<td>Lymph Node Metastases</td>
<td>Yes</td>
</tr>
</tbody>
</table>
INNOVATIVE RADIOTherAPY TECHNIQUES: A MULTICENTRE TIME-DRIVEN ACTIVITY-BASED COSTING STUDY
average cost SBRT: 6,221€

- Free breathing - center A
- Free breathing - center B
- Free breathing - center C
- Free breathing - center D
- Free breathing - center E
- Free breathing - center F
- Gating - center G
- Gating - center H
- Tracking - center I
- Tracking or Free breathing - center J

Hulstaert et al, Report 198 KCE 2013
4-year provisional financing of SBRT prospective evaluation real-life setting

Which departments?
Which indications?
Which technology?
What standards of care?
What outcome?
What budget?
the sky is not the limit
cost-effectiveness is not enough
budget impact is equally relevant
many unsolved issues
focus on evidence and value
provisional reimbursement models