Multi-Comparator ICERs in Cost-Effectiveness Analysis to Account for Changes in Clinical Practice After the Introduction of a New Technology

Authors: Hughes R¹, Lucherini S², Crossley A¹, Okhuoya P¹
Affiliations: ¹Adelphi Values PROVE, Manchester, United Kingdom

Background and Objectives

- Cost-effectiveness analysis (CEA) informs healthcare decision-making in some European countries. For policymakers, it is important to make decisions based upon data as close to clinical practice as possible.
- Traditional CEA methodology estimates the incremental benefits and costs of a proposed new therapy via a pairwise comparison with a single comparator. Typically, this is the most commonly used or most cost-effective comparator.¹
- However, the choice of this single comparator varies between health technology assessment (HTA) bodies,² and selection criteria for an individual HTA body is not always clear, varying between indications.³ Some single comparator choices have been controversial.⁴
- For most indications, a new therapy entering the market takes market share from, or ‘displaces’, a range of existing therapies. Therefore, a pairwise comparison with a single alternative may not capture the full value of introducing a new therapy.
- A new CEA approach could demonstrate the value of a new therapy in context, acknowledging the current misallocation of resources away from the theoretical optimum. By evaluating the market displacement for an indication, a new framework may provide an estimate closer to the true value of a new therapy, as realised in clinical practice.
- A multi-comparator model, accounting for the changing market landscape of a disease area, reflects changes to clinical practice upon entry of a new therapy. This may better inform decision makers, and could help address any allocative inefficiencies in the market, as well as disagreement over single comparator choice in traditional CEA.

Methods

Traditional cost-effectiveness modelling
- Traditional pairwise incremental cost-effectiveness ratios (ICERs) between new therapy and each of its comparators were estimated. A cost-effectiveness frontier was formed to select the appropriate comparator product, via elimination of strictly dominated and extendedly dominated comparators.⁵

Multi-comparator modelling
- Market share data representing the market with and without the new therapy were used. These were counterfactual to each other.
- A multi-comparator ICER (MC-ICER) reflected the change in clinical practice from the displacement of the new therapy. The MC-ICER is the ICER of the new therapy with respect to all displaced comparators, including those which would be excluded as dominated in traditional CEA.
- This was based on a weighted pairwise ICER between the new therapy and each displaced comparator (i.e. without elimination of dominated comparators). The weighting applied to each ICER was based upon the proportion of the total market share change:

\[
\text{MC-ICER} = \frac{\sum_{i} \text{Weight}_i \times \text{ICER}_i}{\sum_{i} \text{Weight}_i}
\]

Example
- The example used data relating to the introduction of brodalumab for the treatment of moderate-to-severe plaque psoriasis in the United States. Table 1 shows the market share data, and relative weight applied to each displaced comparator. It also gives the cost and QALY estimates for each displaced comparator, used in both traditional pairwised CEA, and the MC-ICER calculation.²

Table 1. Market shares, relative weights, costs and QALYs²

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Market share</th>
<th>Relative weight</th>
<th>Cost</th>
<th>QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brodalumab</td>
<td>0%</td>
<td>18%</td>
<td>$240,308</td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>51%</td>
<td>14%</td>
<td>$208,081</td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>17%</td>
<td>12%</td>
<td>$198,598</td>
<td></td>
</tr>
<tr>
<td>Secukinumab</td>
<td>4%</td>
<td>4%</td>
<td>$224,287</td>
<td></td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>14%</td>
<td>12%</td>
<td>$231,704</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>100%</td>
<td>$209,663</td>
<td></td>
</tr>
</tbody>
</table>

Results

Traditional Cost-Effectiveness Analysis
- Table 2 shows the traditional ICERs after eliminating all dominated comparators – adalimumab and ustekinumab. Using traditional CEA methodology, the most appropriate single comparator for brodalumab would be secukinumab. The traditional ICER between brodalumab and secukinumab was estimated at $140,556.
- At a cost-effectiveness threshold of $100,000,⁶ secukinumab would be selected as the optimal therapy. At a threshold of $150,000,² brodalumab would be the optimal therapy instead.

Using the Multi-Comparator ICER
- The MC-ICER is the ICER of brodalumab with respect to all comparators, given the relative weights applied, including those which would be excluded as dominated in traditional CEA.
- The MC-ICER capturing the overall impact on clinical practice was estimated at $50,709 (Table 3).

Conclusions

- The estimated MC-ICER accounting for the overall impact of introducing brodalumab for the treatment of moderate-to-severe psoriasis was $50,709. This was significantly lower (64%) than the $140,556 ICER between brodalumab and secukinumab produced in a traditional CEA.
- The difference between the MC-ICER and the traditional pairwise ICER arises when a new therapy is expected to displace therapies that are less cost-effective than the single comparator in the traditional CEA. It may be interpreted as the value of a product missed in traditional CE estimates, due to omission of other displaced comparators in the final calculation. The larger this difference, the greater the need to support traditional CE evidence with the multi-comparator result in reimbursement discussions.
- In reality, there are many reasons why patients would be prescribed the cost and dominated comparators. If a dominated comparator was used within clinical practice (such as the market leader adalimumab, in the example) is excluded from the analysis, a significant proportion of the value of the new therapy is not accounted for in the decision-making process.
- Although the MC-ICER does require market share data for all the comparators in the market, these are already required for budget impact analysis in many HTA submissions. By taking into account market share changes, the MC-ICER methodology parallels the approach used in budget impact analysis. This is also better aligned to the decision problem faced for reimbursement decisions – most indications have several drugs with market share, not just the single comparator used for the ICER in traditional CEA.
- As the framework also produces traditional ICER estimates, the MC-ICER framework would likely support this analysis by showing payers and policymakers a better estimate of the overall impact of new therapeutic on clinical practice, compared to traditional analysis.
- By taking into account displaced comparators, the MC-ICER methodology would likely incur less degradation over comparator choice than for traditional CEAs.


References


www.adelphivalues.com