Scale Loss Score (SLoS): a novel measure of drug benefit-risk assessment

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Introduction

- MultiCriteria Decision Analysis (MCDA) is a popular quantitative method to assess the benefit-risk (BR) balance of treatments: it permits to summarize the benefits and the risks of a drug in a single utility score.
- The utility score is often derived using a linear model, which might lead to counter-intuitive conclusions, for example, a recommendation of a non-effective drug.
- We propose Scale Loss Score (SLoS) as a new tool for benefit-risk assessment: it is based on strong theoretical principles, addresses the issues of the linear MCDA model and can lead to more meaningful recommendations.

Notations

\[ u_j(\xi_j) : \text{linear partial value functions - map the performances on criterion } j \text{ to a } (0, 1) \text{ scale} \]

\[ u_j(\xi_j) = \frac{\xi_j - \xi'_j}{\xi''_j - \xi'_j}, \xi'_j \text{ and } \xi''_j \text{ the worst and best values} \]

\[ w_j \text{ and } w'_j : \text{weight reflecting the importance of criterion } j \]

Linear MCDA

MCDA linear utility score:

\[ u(\xi, w) := \sum_{j=1}^{n} w_j u_j(\xi_j) \]

Higher utility score → more preferable BR balance

Contour of \( 1 - u(\xi_1, \xi_2, w = 0.5) \)

- Benefit-risk trade-off is the same for all values of risk / benefit.
- Drugs with no benefit or extreme risk can be recommended.

SLoS

Scale Loss Score (SLoS):

\[ l(\xi, \tilde{w}) := \sum_{j=1}^{n} \left( \frac{1}{u_j(\xi_j)} \right)^{\tilde{w}_j} \]

Lower loss score → more preferable BR balance

Contour of \( l(\xi_1, \xi_2, \tilde{w} = 0.5) \)

- For a given increase in benefit, a smaller increase in risk is tolerated if benefit is high than if it is low.
- Drugs with no benefit or extreme risk can never be recommended.

Examples

Fictive examples

2 criteria, fixed parameter values and \( w = \tilde{w} = 0.25 \)

<table>
<thead>
<tr>
<th></th>
<th>Example 1</th>
<th>Example 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug 1 Benefit</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Drug 1 Risk</td>
<td>9%</td>
<td>20%</td>
</tr>
<tr>
<td>Drug 2 Benefit</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>Drug 2 Risk</td>
<td>0%</td>
<td>20%</td>
</tr>
</tbody>
</table>

- SLoS strongly penalizes extremely low benefit values and extremely high risk values.

Case study: telithromycin

IMI PROTECT Benefit-Risk Group example

Proba(telithromycin > \beta-lactam antibiotics)

<table>
<thead>
<tr>
<th>Community Acquired Acute Bacterial Pneumonia (CAP)</th>
<th>Sinusitis (ABS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCDA</td>
<td>SLoS</td>
</tr>
<tr>
<td>59%</td>
<td>51%</td>
</tr>
<tr>
<td>71%</td>
<td>55%</td>
</tr>
</tbody>
</table>

→ SLoS results are more in line with the regulatory authorities concerns on ABS indication (CHMP reassessment and FDA removal).

Conclusion

Results of simulations comparing MCDA and SLoS:

- Both are robust to correlations between outcomes.
- Similar conclusions in many cases.
- Clear advantage of SLoS when drugs have no benefit or extreme risk.

Scale Loss Score (SLoS) is a novel, simple and valuable tool for BR assessment.