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

- \(\xi_j\): performance of treatment \(i\) on criterion \(j\), \(j = 1, \ldots, n\)
- \(u_j(\xi_j)\): linear partial value functions - map the performances on criterion \(j\) to a \((0,1)\) scale
- \(u_j(\xi_j) = \frac{\xi_j - \xi_j^\prime}{\xi_j^\prime - \xi_j^\prime}\), \(\xi_j^\prime\) and \(\xi_j^\prime\) the worst and best values
- \(w_j\) and \(\tilde{w}_j\): 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 \(\rightarrow\) more preferable BR balance

Case study: telithromycin

IMI PROTECT Benefit-Risk Group example

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

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

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 \(\rightarrow\) more preferable BR balance

Examples

- **Fictive examples**
  - 2 criteria, fixed parameter values and \(\tilde{w}\) = \(\tilde{w}\) = 0.25
  - Example 1
    - Low benefit and risk
    - Drug 1: Benefit 0% Risk 20% Drug 2: Benefit 100% Risk 85%
  - Example 2
    - High benefit and risk
    - Drug 1: Benefit 90% Risk 30% Drug 2: Benefit 50% Risk 90%

- **Case study: telithromycin**
  - IMI PROTECT Benefit-Risk Group example
  - Proba(telithromycin > β-lactam antibiotics)
  - Community Acquired Acute Bacterial Pneumonia (CAP) | Sinusitis (ABS)
  - MCDA: 59% | 71%
  - SLoS: 51% | 55%

- \(\rightarrow\) SLoS strongly penalizes extremely low benefit values and extremely high risk values

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

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