Integrating elicited patient preferences and clinical trial data in a quantitative model for benefit-risk assessment

Henk Broekhuizen, MSc1; Karin Groothuis-Oudshoorn, PhD2; Brett Hauber, PhD2; J.P. Jansen, PhD2; Maarten IJzerman, PhD1

1 University of Twente, dept. Health Technology and Services Research, Enschede, the Netherlands
2 RTI Health Solutions, Research Triangle Park, NC, USA
3 MAP Group, Boston, MA, USA

Objectives
Demonstrate how elicited patient preferences can be integrated in a Bayesian framework for quantitative benefit-risk assessment.

Methods
We identified models that can be used to integrate preference and performance information in quantitative benefit-risk assessment models and evaluated if they would be suitable for elicited patient preferences. Based on our findings we developed a model.

Results
• Identified models: discrete event simulation and multi criteria decision analysis (MCDA): found limitation: uncertainty around patient preferences not taken into account.
• We therefore developed a Bayesian MCDA model, with
• Antidepressants used as illustrative case.

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
<th>Response</th>
<th>Remission</th>
<th>Adverse events</th>
<th>Severe adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine’s Benefit-risk ratio</td>
<td>0.16 (0.07 to 0.34)</td>
<td>0.16 (0.07 to 0.34)</td>
<td>0.04 (0.01 to 0.23)</td>
<td>0.19 (0.02 to 0.25)</td>
<td></td>
</tr>
<tr>
<td>Duloxetine’s Benefit-risk ratio</td>
<td>0.88 (0.71 to 1.08)</td>
<td>0.88 (0.71 to 1.08)</td>
<td>0.56 (0.40 to 0.72)</td>
<td>0.62 (0.45 to 0.78)</td>
<td></td>
</tr>
<tr>
<td>Bupropion’s Benefit-risk ratio</td>
<td>0.30 (0.24 to 0.36)</td>
<td>0.30 (0.24 to 0.36)</td>
<td>0.36 (0.30 to 0.41)</td>
<td>0.36 (0.30 to 0.41)</td>
<td></td>
</tr>
<tr>
<td>Remission weight</td>
<td>0.70 (0.60 to 0.80)</td>
<td>0.70 (0.60 to 0.80)</td>
<td>0.60 (0.50 to 0.70)</td>
<td>0.60 (0.50 to 0.70)</td>
<td></td>
</tr>
<tr>
<td>Adverse events weight</td>
<td>0.10 (0.05 to 0.15)</td>
<td>0.10 (0.05 to 0.15)</td>
<td>0.10 (0.05 to 0.15)</td>
<td>0.10 (0.05 to 0.15)</td>
<td></td>
</tr>
<tr>
<td>Severe adverse events</td>
<td>0.05 (0.02 to 0.08)</td>
<td>0.05 (0.02 to 0.08)</td>
<td>0.05 (0.02 to 0.08)</td>
<td>0.05 (0.02 to 0.08)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: The MCDA model structure, comparing Duloxetine (Dul), Venlafaxine (Ven) and Bupropion (Bup) on two benefit criteria and two risk criteria.

Figure 2: Risk-benefit plane with overall drug scores. Line v denotes where the sum of the weighted benefits equals the sum of the weighted risks. All simulation runs are below v, which means all drugs’ benefits outweigh their risks. This implies all drugs are acceptable.

Figure 3: (top row) Estimated densities of the weighted benefit performances, weighted risk performances and benefit-risk ratios of all drugs, and (bottom row) rank probabilities for weighted benefit performances, weighted risk performances and benefit-risk ratios. Green=first rank, blue-second rank and red-third rank.

Figure 4: Example sensitivity graph that shows the sensitivity of Venlafaxine’s benefit-risk ratio to the weights assigned to criteria by patients. The vertical grey lines denote the weights’ 95% credibility interval. As expected, its benefit-risk ratio increases with the response criterion and decreases with the risk criterion. It is not sensitive to the weight for remission.

Conclusions
• Elicited patient preferences used to weigh drugs’ clinical performance data
• Integrates uncertainty around patient preferences and clinical performance.

Strengths
• All data structured in one comprehensive model
• Impact of uncertainty and robustness of decision can be checked
• Visualization of data and uncertainty

Limitations
• Structural model assumptions
• Only first order uncertainty considered
• Inconsistent sampled pairwise comparison matrices for severe adverse events criterion

Future research
• Regulators’ requirements vs patient preferences
• Other types of preferences studies
• Using mixed treatment comparison data

Contact information:
h.broekhuizen@utwente.nl
www.utwente.nl/staff/hbroekhuizen.doc