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

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Introduction:
Regulators increasingly incorporate patients’ view on benefit-risk tradeoffs but little is known on how to integrate elicited preferences into the quantitative models. There is little knowledge on how to integrate these preferences with clinical performance data and how to use knowledge about the uncertainty surrounding both types of parameters (preference and performance).

Methods:
An MCDA model was developed that integrates clinical trial data, elicited patient preferences and uncertainty surrounding these estimates. Stochastic characteristics of preference and drug performance parameters can be approximated from stated preference studies and performance data from systematic reviews or RCT’s. Risk and benefit scores of drugs are then simulated with Monte Carlo methods using approximated distributions.

Results:
The model was applied to an anti-depressants case. We included two benefit and one risk criteria (figure 1). Preference data was derived from an analytical hierarchy process study with 12 major depression disorder patients who were currently in remission and the performance data (pooled odds ratio’s compared to placebo) were derived from a systematic review. The distribution around preferences was approximated with a bootstrap method, the distribution around performance data was approximated with a normal distribution in the log domain. The simulations show all drugs have high (=1) acceptabilities (figure 2). The problem is more sensitive to performance information than to preference information and most sensitive to the adverse events performance criterion.

Figure 1: MCDA structure for the antidepressants case.

Figure 2: Risk-benefit plane. All simulation runs are below the $\mu=1$ threshold and are thus acceptable.

Figure 3: A value sensitivity graph for the adverse events weight and drug A (left). A decision sensitivity graph for drug A (middle). A ranking sensitivity graph for drug B and its performance on the response criterion (right). In the ranking sensitivity graph, the green line is drug B’s probability of being rank=1, blue of rank 2 and red of rank 3. In all graphs, the two black vertical lines denote the 95% CI of the parameter on the x-axis.

Conclusion:
Using this MCDA model it is possible to include patient preference in a quantitative risk-benefit assessment model. The model allows integration of stochastic uncertainty concerning preference and performance. It demonstrates that comprehensive presentation of data is possible.