Shifting from risk aversion to risk awareness in drug reimbursement processes in the Netherlands

HPR122

J. Severens[1], M. Postma[2], M. Sculpher[3]

1. Severens HTA Consultancy, Heemskerk, Netherlands 2. University of Groningen, Groningen, Netherlands
3. University of York, York, United Kingdom

INTRODUCTION

- The effectiveness of novel, more expensive technologies is essential for reimbursement decisions.
- Incremental clinical effectiveness is often benchmarked against the minimal important difference (MID).
- For oncology drugs, the Dutch Healthcare Institute ZIN) assesses the hazard ratio (HR) for overall survival of a new treatment versus standard of care.
- The Dutch clinical PASKWIL criteria state that the HR for OS should be below 0.7 to be considered clinically relevant.

CURRENT APPROACH

- In the Netherlands, a stepwise approach is being used: 1) regarding effectiveness ("established medical science and medical practice", SW&P) and 2) cost-effectiveness of a novel technology.
- Not reaching a statistically significant improvement in the MID, may lead to down-grading the evidence regarding effectiveness, a qualitative manner to handle uncertainty.
- In case effectiveness is defined insufficient, cost-effectiveness is not assessed within the drug reimbursement decision making process.
- The cost-effectiveness threshold of 80,000 €/QALY represents opportunity costs.

OBJECTIVE

This study explores the value of decision analysis and risk awareness in drug reimbursement decision-making, using an integrated, quantitative approach of assessing clinical effectiveness and cost-effectiveness, in comparison to the current qualitative stepwise approach in the Netherlands.

METHODS

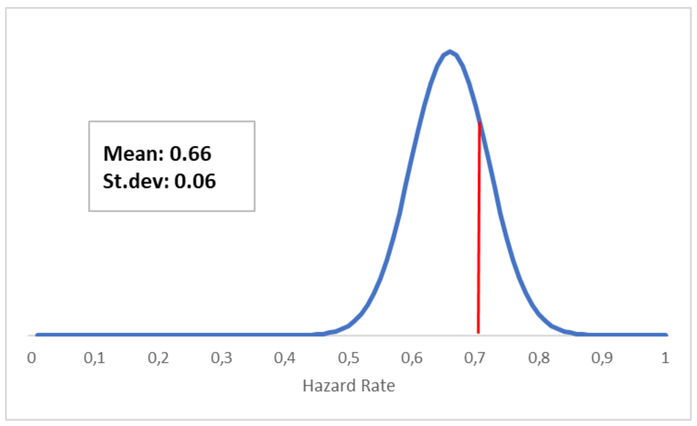
- Based on decision analysis we compare the current stepwise, qualitative approach in reimbursement decision making vs. an integrated, quantitative approach.
- Our integrated approach incorporates statistical uncertainty regarding clinical effectiveness in a quantitative manner.
- This approach makes explicit:
  1. the probability of making the right (true) of wrong (false) decision, given the statistical uncertainty of the HR in relation to the MID:
     The probabilities of true or false reimbursement decision are derived from the distribution of HR and the definition of MID.
  2. the consequences of a right and wrong reimbursement decision:
     For negative and positive reimbursement decisions, either being false or true, corresponding QALY's and cost for the new treatment (experimental) and standard of care (control) are used to calculate the NHB.

HYPOTHETICAL EXAMPLE

Effectiveness:

Given: Hazard Ratio of Overall Survival:
- Mean: 0.66
- Standard error of the mean: 0.06
- HR-95%CI: 0.54 – 0.78

Calculated: probability the HR meets the MID:
- Defining he distribution of HRs
- Defining the proportion of the distribution of HRs below the MID
- **Result**: probability HR < 0,7: ~74%



A reimbursement decision can be true or false, considering the statistical uncertainty of the HR in relation to the MID.

Cost-Effectiveness:

	Experimental	Control	Incremental
Average cost	€ 130,000	€ 90,000	€ 40,000
Average effect	QALY 2.0	QALY 1.4	QALY 0.6
ICER			€/QALY 66,667
CE-threshold			€/QALY 80,000
Net Health Benefit	€ 30,000	€ 22,000	
Incremental NHB			€ 8,000

RESULTS

Negative reimbursement decision

True negative:
- **Cost: 90,000€**
- **Effect: 1,4 QALY**
- **NHB: 22,000€**

False negative:
- **Cost: 90,000€**
- **Effect: 1,4 QALY**
- **NHB: 22,000€**
- **Opportunity costs of wrong decision: 8,000€**

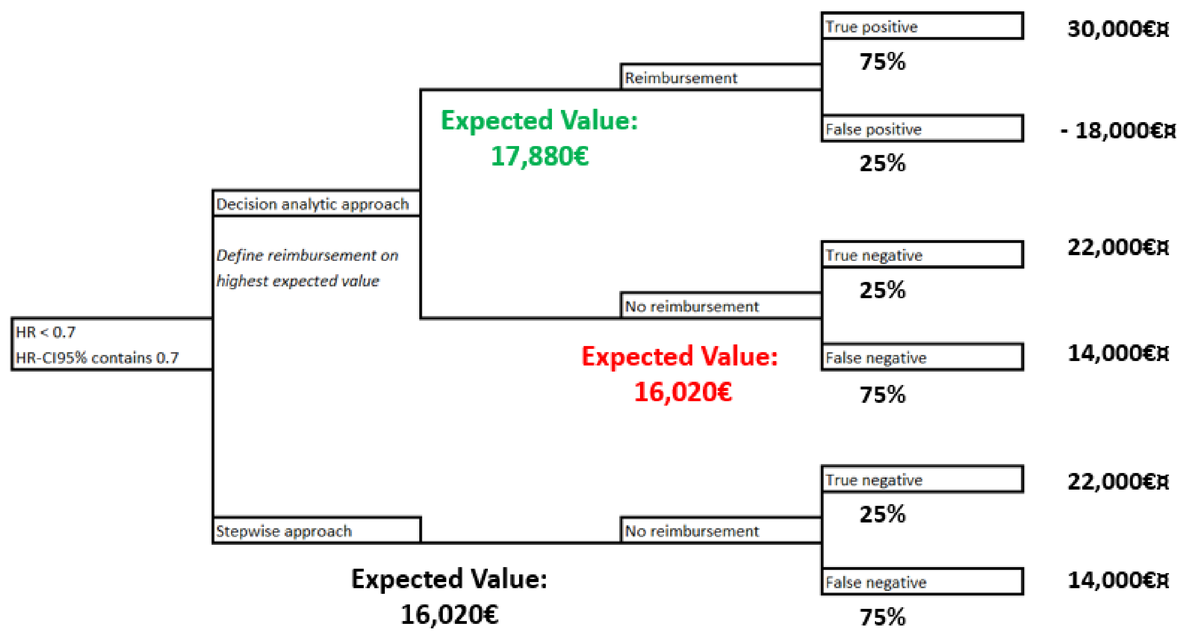
Positive reimbursement decision

True positive:
- **Cost: 130,000€**
- **Effect: 2 QALY**
- **NHB: 30,000€**

False positive:
- **Cost: 130,000€**
- **Effect: 1.4 QALY**
- **NHB of wrong decision: - 18,000€**

= (qaly control*CE-threshold) - cost experimental

The values of true and false decisions, either being positive or negative are based on net health benefit calculation.



A decision tree combines values with the probabilities of a right or wrong reimbursement decision. The stepwise, qualitative approach is compared to the alternative decision analytic approach where cost-effectiveness is considered, also in case reaching the MID is statistically uncertain.

CONCLUSIONS

- In our hypothetical example, despite statistical uncertainty regarding the MID, a positive reimbursement decision leads to the highest expected value compared to no reimbursement.
- A stepwise, qualitative approach to first assessing clinical effectiveness and depending on a positive conclusion, as a second step, estimating cost-effectiveness, may therefore result in suboptimal reimbursement decisions.
- An integrated, quantitative approach of dealing with statistical uncertainty of effectiveness in relation to a MID leads to decision making based on the highest expected NHB.

Decision-makers in the Netherlands should shift from being risk averse to becoming risk aware in case the MID does not reach statistical significance.

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DISCLOSURES AND CONTACT INFORMATION

For this research J. Severens was supported by an unrestricted grant of AstraZeneca Nederland B.V. The views presented are based on the personal opinions of the authors.

Severens HTA CONSULTANCY

Corresponding author: hans.severens@severenshta.eu