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The Impact of Decision Makers' Constraints on the Outcome of Value of Information Analysis

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ABSTRACT

Background: When proven effective, decision making regarding reimbursement of new health technology typically involves ethical, social, legal, and health economic aspects and constraints. Nevertheless, when applying standard value of information (VOI) analysis, the value of collecting additional evidence is typically estimated assuming that only cost-effectiveness outcomes guide such decisions. **Objectives:** To illustrate how decision makers' constraints can be incorporated into VOI analyses and how these may influence VOI outcomes. **Methods:** A simulation study was performed to estimate the cost-effectiveness of a new hypothetical technology compared with usual care. Constraints were defined for the new technology on 1) the maximum acceptable rate of complications and 2) the maximum acceptable additional budget. The expected value of perfect information (EVPI) for the new technology was estimated in various scenarios, both with and without incorporating these constraints. **Results:** For a willingness-to-pay threshold of €20,000 per quality-adjusted life-year, the probability that the new technology was cost-effective equaled 57%, with an EVPI of €1,868 per patient. Applying the complication rate constraint reduced the EVPI to €1,137. Similarly, the EVPI reduced to €770 when applying the budget constraint. Applying both constraints simultaneously further reduced the EVPI to €318. **Conclusions:** When decision makers explicitly apply additional constraints, beyond a willingness-to-pay threshold, to reimbursement decisions, these constraints can and should be incorporated into VOI analysis as well, because they may influence VOI outcomes. This requires continuous interaction between VOI analysts and decision makers and is expected to improve both the relevance and the acceptance of VOI outcomes.

Keywords: decision making, multiple constraints, reimbursement, research prioritization, value of information.

Introduction

After effectiveness has been demonstrated, decisions on reimbursement of new health technologies in most Western European countries are based on, among others, ethical, juridical, social, and health economic considerations. Examples of such considerations are maximum budget impact, maximum complication rates (CRs), minimum overall health benefits, and health equity. Currently, the interest in the application of health technology assessment with explicit and transparent incorporation of multiple constraints or decision criteria is increasing [1–4]. Methods for explicating and valuating constraints have been developed [5–7], and various approaches to decision making on the basis of multiple constraints exist [8–10].

When decision makers consider new technology (NT) they typically have more options than immediately approving or rejecting. For example, a decision maker might consider supporting or reimbursing an NT "only in research" or "approved with research" [11,12]. Such decisions can be informed by evaluating the current uncertainty surrounding the health economic results, and determining the value of reducing that uncertainty, to improve decision making in a value of information (VOI) analysis [13–15]. Here, it is recognized that the collection of additional evidence to enhance the decision outcome may be affected by the reimbursement decision itself. For example, full unconditional reimbursement of an NT may make it hard to collect new evidence on current usual care (UC) if the NT would rapidly replace current care in clinical practice. This challenge can be addressed by separately assessing the expected impact of "only in research" and "approved with research" decisions, as alternatives to an "approve or reject" decision, and determining the optimal decision from this set. Nevertheless, constraints arising from any of the considerations mentioned are typically not included in the VOI analysis and are also not incorporated

Conflicts of interest: The views expressed in this article are those of the authors and should not be attributed to the authors' respective employers.

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into this wider set of possible decisions. In other words, VOI outcomes are mostly derived considering that policy decisions are determined by cost-effectiveness outcomes only.

In this article we illustrate how explicit additional constraints on the acceptability of new health technology may be incorporated into VOI analysis, and how this may affect VOI outcomes.

Methods

We assessed the impact of two plausible constraints on the reimbursement decision regarding a new hypothetical health technology in a simulation study. In this study we compare costs and effects of the NT with UC.

Outcomes of the NT and UC

We evaluated the cost-effectiveness of an NT compared with UC. Mean costs were set to €8,000 ± 1,000 for UC and €10,000 ± 2,000 for NT. Mean effects were expressed in quality-adjusted life-years (QALYs) and set to 0.45 ± 0.30 for UC and 0.60 ± 0.20 for NT. In addition, the CRs for UC and the NT were set to 2.75% (0.15%) and 2.75% (0.55%), respectively. Here, the impact of complications from use of the NT, or UC, was assumed to be included in the respective cost and effect outcomes. Correlations were defined between the costs and effects and between the CRs and effects (separately for NT and UC) as well as between the effects of NT and UC. The Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2017.04.011 contain a table with an overview of all simulation parameters, including the ensuing correlations between all parameters and the source code used for the simulations. Uncertainty in costs, effects, and risk of CRs was simulated using multivariate normal distributions with mean and SD as indicated (1,000,000 samples).

Description of the Constraints

We applied a cost-effectiveness threshold of €20,000 per QALY gained as health economic constraint, a threshold that is commonly referred to in the Netherlands [16]. In addition, we defined a constraint regarding the maximum acceptable CRs. This constraint was represented by an absolute threshold of 3% CR for the NT. This threshold could represent advice from medical professionals and patient organizations regarding the maximum clinically acceptable CRs. If evidence would suggest that the expected CR for the NT exceeds this threshold, it would not be considered an acceptable alternative to UC. This would apply regardless of 1) the cost-effectiveness of the NT and 2) the CR of UC (which have been deemed acceptable in the past, even though this rate may exceed the CR threshold currently set for the NT). Finally, we also defined a constraint on the maximum *additional* costs incurred by NT compared with UC. Here, the threshold was set to €2,500. Combined with, for example, a potential target population of 1,000 individuals eligible to receive the NT, this would correspond to a maximum additional budget of €2,500,000. New technologies exceeding such a budget increase require further and more detailed analysis in the Netherlands.

Calculating the VOI Outcomes and Decision Options

To derive the expected VOI we started by calculating the net monetary benefit (NMB) for both alternatives. Next, the NMB for both alternatives was calculated per sample separately. The current best option was determined by selecting the alternative with the highest expected NMB. The expected value of perfect information (EVPI) was determined by first selecting the alternative with the highest expected NMB, separately for each sample, and then subtracting the expected NMB of the current best option from the expected NMB of selecting the best option per sample [17,18].

Calculating the VOI When Constraints Apply

In case constraints apply, a decision maker might still prefer UC over NT even when the *expected* CR or *expected* additional costs for NT do not exceed the constraint threshold(s), but the *risk* of exceeding a threshold(s) is deemed to be substantial. Such a "risk-averse" attitude would render UC to remain the preferred option despite potential benefits of NT. In our example we presumed that a risk-averse decision maker would not prefer NT in case the risk of exceeding constraint thresholds would be more than 30%. Note that this is an arbitrary threshold value.

For the calculation of the EVPI in our example, a Monte-Carlo simulation was performed in which 1,000,000 samples were drawn. Constraints were applied for CRs and the maximum additional costs for NT. From these samples the expected NMB and the threshold exceedance probabilities were calculated for both NT and UC, and the best option was determined. The best option was again determined but now separately for each sample. Finally, the EVPI was calculated from the difference in NMB of the best option across all samples and the expected NMB of the best options per sample. To calculate the EVPI while applying constraints, the following six steps were taken; Table 1 provides an illustration of these steps performed for five random samples.

1. Calculate the expected NMB for NT and UC and the risk of exceeding the constraint threshold.
2. Determine the best option, that is, the alternative with the highest NMB that complies with the applicable constraints and with an acceptable risk of exceeding these constraints.
3. Determine for each sample whether NT complies with specified constraint(s).
4. For each sample define the highest *acceptable* NMB as:
   a. the NMB of UC in case of noncompliance of NT with the applicable constraint(s);
   b. the highest NMB of UC and NT in case of compliance of NT with the applicable constraint(s).
5. Calculate the expected highest acceptable NMB over all samples.
6. Subtract the expected NMB of the current best option (step 2) from the expected highest acceptable NMB (step 5).

Note that if multiple constraints are applied, all constraints have to be met by the NT in step 4a of the analysis before its NMB is even compared with the NMB of UC. Also, in case the expected NMB of NT is higher than that of UC the EVPI for the risk-averse decision maker will increase by the difference between the expected NMB of NT and that of UC because this is the benefit the additional information provides by opening up the possibility of actually implementing NT.

All calculations were performed using the statistical package R version 3.3.1 (The R Foundation for Statistical Computing, Vienna, Austria) [19].

Results

Figure 1 shows the incremental cost-effectiveness plane for NT compared with UC. The expected difference in health outcomes equals 0.15 QALYs; the difference in costs is expected to be €2000. The NMB of UC equals €1000 per patient, whereas the NMB of NT equals €2,000 per patient. Therefore, NT is expected to be preferred over UC, given this cost-effectiveness threshold. Current evidence, however, indicates that it is rather uncertain