Enhancing Value of Information Analyses

Mart P. Janssen, MSc, Hendrik Koffijberg, PhD
Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

**ABSTRACT**

Objective: The aim of this study was to demonstrate that it is feasible and recommendable to present value of information (VOI) outcomes in terms of underlying costs and effects in addition to costs alone.

Methods: The benefits of collecting additional information on health economic outcomes before deciding on a preferred policy when evaluating alternative strategies with uncertain outcomes are quantified in a VOI analysis. In general, costs and effects are combined into one single dimension to determine the expected monetary VOL. Separate information on costs and effects is lost. This information, however, remains relevant to the decision-maker. The concept of the attributable VOI (AVOI) is introduced which enables separate presentation of expected changes in health outcomes and costs.

Results: The use of the attributable expected value of perfect information is illustrated with a few examples. These examples demonstrate the benefits of the new approach, as well as its calculation. The benefits are: 1) insight into the expected costs and expected effects gained as a result of carrying out further research to reduce or eliminate decision uncertainty; and 2) the likelihood that the outcome of additional research will result in a change in preferred policy.

Conclusions: Decision-making may be enhanced and clarified by adding results from AVOI analyses. Obtaining these results is straightforward and requires only a minimal computational effort. Therefore, use of the AVOI extension is recommended for all future VOI analyses.

Keywords: attributable value of information, decision uncertainty, economic evaluation, simulation.

Introduction

With the continuous rise of health-care costs, efficiency of health care and health-care research is becoming increasingly important. Value of information (VOI) analyses allows a systematic quantification of the expected financial gain from additional information for decisions made under uncertainty. These kinds of analyses are increasingly applied in health policy research and health technology assessment [1–5]. VOI outcome is proposed as a measure for setting priorities on additional research among research projects, as it indicates a project’s potential for return on investment. Nevertheless, there is a price to be paid for obtaining the VOI. In a conventional comparison of health-care interventions, outcomes are projected in a cost-effectiveness plane, giving information on incremental costs and effects for all interventions. Calculating the VOI is done within a net monetary benefit (NMB) framework. Within this framework, the setting of a particular cost-effectiveness threshold (CET) is defined which provides a means for valuating health effects in terms of their monetary equivalent. This enables a decision on the preferred intervention for any combination of intervention outcomes. This is the one with the highest monetary equivalent (i.e., the highest NMB). Nevertheless, as costs and effects are combined into one single dimension, information on each of the separate dimensions is lost. This information, however, can be—and we will argue that it is—relevant to the decision-maker.

We develop the concept of “attributable VOI” (AVOI). The AVOI is a straightforward extension of the general VOI concept whereby it is split into separate parts for costs and effects that add up to the total VOI. We will demonstrate and apply this concept to the measure of expected value of perfect information (EVPI). The AVOI allows the decision-maker to judge not only the value of additional research, but also its impact in terms of the expected shift in costs and effects as compared to the currently preferred intervention. These additional insights improve a decision-maker’s ability to evaluate the merits of additional research.

Methods

**Standard EVPI**

Measures such as the EVPI and the expected value of sample information (EVSI) may be used for research prioritization, based on comparisons between expected benefits and costs of future research projects [6]. The EVPI was introduced in the 1960s and has a straightforward interpretation: It is the difference between the expected utility of the decision when no uncertainty exists (perfect information) and expected utility of the decision based upon current evidence [7]. In a health economic context, effects are usually expressed in terms of quality-adjusted life-years (QALYs). Subsequently, the NMB is used to determine the utility of a particular outcome of an intervention [8]. The NMB (Equation 1) is a simple linear function of the CET, costs (C in $), and effects (Q in QALYs). The preferred intervention is the one with the highest expected NMB. The EVPI as function of the CET over all interventions j with respect to the parameter space Ω of costs and effects (with realizations ω) is given by Equation 2.

\[
\text{NMB}(j, ω, \text{CET}) = \text{CET} \cdot Q(j, ω) - C(j, ω)
\]  

(1)

\[
\text{EVPI}(j, ω, \text{CET}) = E_ω[\text{NMB}(j, ω, \text{CET})] - \text{max} \{E_ω[\text{NMB}(j, ω, \text{CET})]\}
\]  

(2)

For each intervention, the bivariate (correlated) distribution of intervention outcomes (costs and effects) is required for the calculation of the EVPI. The second part of Equation 2 refers to the mean NMB for each of the interventions considered. Conversely, the first part of this equation refers to the mean of the
maximum) NMB for each potential combination of outcomes separately. This mimics the situation where the best decision is taken in each viable situation.

Despite the simple form of Equation 2, it does not reveal any characteristics of the EVPI. For example, it does not reveal how the EVPI is affected by differences in costs and effects between interventions and their dispersion. This complicates the understanding of the EVPI at the basic level: EVPI values cannot be interpreted in terms of costs and effects.

**EVPI and the Segregation of Costs and Effects**

The transformation of intervention outcomes to an NMB is required to decide on the preferred intervention, which is the one with the highest expected NMB. In the calculation of the EVPI, the outcome of either intervention is expressed in the NMB which results in a monetary equivalent in which the EVPI is expressed. Nevertheless, as the NMB in Equation 2 for any given $j$ and $\omega$ is calculated using Equation 1 with specific cost-and-effect outcomes, the contribution of costs and effects to the EVPI can be separated. This only requires taking the respective costs or effects associated with the intervention that maximizes the NMB.

By doing this, the attributable costs (Equation 3a) and attributable effects (Equation 3b) of the EVPI are obtained.

$$AEVPICost(j, \omega, CET) = E_C\{f_C[\max\{NMB(j, \omega, CET)\}] - f_C[\max\{E_C\{NMB(j, \omega, CET)\}\}]\} \quad (3a)$$

$$AEVPIEffect(j, \omega, CET) = E_E\{f_E[\max\{NMB(j, \omega, CET)\}] - f_E[\max\{E_E\{NMB(j, \omega, CET)\}\}]\} \quad (3b)$$

The functions $f_C$ and $f_E$ in Equation 3 refer to the respective underlying costs and effects associated with the NMB they are applied to. The fact that the NMB is a linear combination of costs and effects implies that the functions $f_C$ and $f_E$ can also be applied to the expected value of the NMB. The results are equivalent to the expected costs and expected effects, respectively. Also, the attributable effects multiplied by the CET minus the attributable costs are equivalent to the EVPI.

**Simulations to Illustrate the Additional Value of the Attributable EVPI (AEVPi)**

To illustrate how the AEVPi can support decision-making, three examples are given. For each example, the standard EVPI and AEVPi are calculated. In addition, a step-by-step illustration of how the AEVPi is calculated will be provided for one of the examples. Calculations were performed using Microsoft Excel® (MS-Excel 2002, Microsoft Corp., Redmond, WA) and R® (version 2.7.2, The R Foundation for Statistical Computing, Vienna, Austria). A fully accessible spreadsheet and R code containing the examples presented in this article can be obtained from the authors upon request.

**Results**

Calculation of the EVPI requires a probabilistic estimation of costs and effects of two interventions and a CET. For both interventions, the distributions of costs and effects are generally presented graphically in a cost-effectiveness plane. Figure 1 shows an example of a cost-effectiveness plane with a generic decision problem concerning two interventions: intervention (1) with expected outcome $P_1$, and intervention (2) with expected outcome $P_2$. The uncertainty in the outcomes of $P_1$ and $P_2$ is visualized as a 95% confidence interval for their respective costs and effects. In this example, costs and effects follow uncorrelated normal distributions. Mean costs and effects, as well as the dispersion of these outcomes, are known: for intervention (1), the mean costs, effects, and 95% confidence contours of two interventions $(P_1$ and $P_2$), their respective expected mean costs, and effects conditional on being the preferred intervention while knowing their exact outcomes $(P_1^*$ and $P_2^*)$, and the expected outcome conditional on perfect information $(A)$. The attributable EVPI is represented by the difference between $A$ and $P_1$, and consists of attributable costs and attributable effects. Intervention (1) ($P_1^*$) is normally distributed with costs $\$1000$ (SD $\$600$) and effects $0.2$ quality-adjusted life-years (QALYs) (SD $0.3$ QALYs). Intervention (2) ($P_2^*$) is normally distributed with costs $\$400$ (SD $\$1000$) and effects $0.1$ QALYs (SD $0.2$ QALYs). The EVPI for this decision problem is $\$2755$; the AEVPICost and AEVPIEffect are $-\$309$ and $0.098$ QALYs, respectively.
mean costs are $1000 with an SD of $600. The mean effect is 0.2 QALYs (SD 0.3 QALYs); intervention (2) has mean costs of $400 (SD $1000) and mean effect of 0.1 QALYs (SD 0.2 QALYs). In Figure 1, a line is drawn through \( P_1 \), which represents a CET of $25,000 per QALY. Any point on this line has an NMB that is equal to that of intervention (1). Given this CET, intervention (1) is the preferred intervention because \( P_2 \) lies above the CET line, which implies that \( P_2 \) has the lesser expected NMB. The expected NMB of intervention (1) equals 0.2 QALYs \( \times \) $25,000 per QALY = $1000 = $4000. The expected NMB of intervention (2) equals 0.1 QALYs \( \times \) $25,000 per QALY = $400 = $2100. Nevertheless, although the expected NMB of intervention (1) exceeds the expected NMB of intervention (2), there is a chance, given the uncertainty in costs and effects of both interventions, that the NMB of intervention (2) is the highest. In that case, intervention (2) is to be preferred. Points \( P_1^* \) and \( P_2^* \) represent the expected costs and expected effects of those outcomes that have either intervention (1) or (2), respectively, as the preferred intervention. Point A indicates the mean costs and effects of the preferred intervention (irrespective of this being (1) or (2)). Point A is the average of \( P_1^* \) and \( P_2^* \), weighting each of these with their respective probability of being the preferred intervention. The cost difference between \( P_1 \) and \( A \) represents the AEVPI cost, whereas the effect difference between \( P_1 \) and \( A \) represents the AEVPI effect. This is the graphical equivalent of Equation 3.

**Example Calculations**

The calculation of the AEVPI is illustrated using the example given in Figure 1. The results are shown in Table 1. This table shows simulated costs and effects for both interventions. Samples were drawn randomly from aforementioned normal distributions. From Table 1, it can be found that the estimated average NMB on the basis of 20 samples is $4371 and $1025 for interventions (1) and (2), respectively (“Sample average” row of columns C and F). Intervention (1) would be (correctly) considered the preferred intervention on the basis of this limited sample. The AEVPI cost (AEVPICost) is estimated at $314 and the AEVPI effect (AEVPIEffect) at 0.084 QALYs. The attributable effect value (i.e., the cost equivalent of the attributable effect (AEVPI\(_{\text{Attrib. Value}}\)), is found by multiplying the attributable effect with the CET (0.084 \( \times \) $25,000 = $2100). Note that the attributable effect value minus the attributable costs is indeed—apart from rounding errors—equal to the EVPI ($2410).

It is common to represent the value of the EVPI graphically as a function of the CET. In Figure 2, this relation is shown for the AEVPI and, in addition, for the attributable cost and attributable effect values. Please note that minus the AEVPICost is shown so that the sum of the AEVPI lines equals the (total) EVPI. From Figure 2 is apparent that for a CET less than $6000 per QALY, both the AEVPI\(_{\text{Effect Value}}\) and AEVPICost are increasing. As the \( -\text{AEVPICost} \) line is declining, the AEVPI\(_{\text{Cost}}\) is increasing. Here, intervention (2) is the preferred intervention. At $6000 per QALY, the decision-maker is indifferent as the expected NMB is equal for both interventions. For larger CET values, intervention (1) is preferred. At a CET of zero, intervention (1) will only be preferred in case it results in lower costs. Therefore, the AEVPICost at this point is negative, and minus the AEVPICost in Figure 2 is positive. As long as there is uncertainty with respect to the sign of the relative effect outcome, the contribution of the AEVPI\(_{\text{Effect Value}}\) to the EVPI will increase with an increasing CET. This is the cause for the unlimited growth found in many EVPI curves. For a CET of $6000 per QALY, the preferred intervention changes. As a result, the AEVPIs show a discontinuity as the outcome reference point (second term in Equations 2 and 3) is no longer the expected outcome of intervention (2), but that of intervention (1). For higher CETs, the EVPI is dominated by the effect outcome, and the AEVPICost becomes dependent on the probability that intervention (2) is more effective than intervention (1). As in this setting, this probability becomes rather insensitive to changes in CET values over $6000 per QALY, the AEVPICost only slowly increases beyond this point.

**Additional Examples**

Two more examples of a decision between two interventions with uncertain outcomes are given in Figures 3 and 4. A summary of the characteristics and the outcomes of all examples is given in Table 2. In Figure 3 (example 2), a situation is given where intervention (2) is shifted upward along the CET line such that the expected effect is doubled. Comparing NMB outcomes between interventions (1) and (2) in this example will therefore give the same results as when comparing NMB outcomes in Example 1. Hence, the EVPI of example 1 is identical to that of example 2, and cannot be used to distinguish between them.

The difference between these two situations, however, is clearly illustrated by the AEVPI. In example 1, the AEVPI costs are $309 whereas in example 2 these are $734. From the presentation in the cost-effectiveness plane, it is clear that the outcome of additional research is likely to result in a preferred strategy which has higher expected costs and effects. EVPI is sometimes presented without information on relative cost-effectiveness of interventions, especially when multiple interventions are compared [9]. On the other hand, when taking decisions on strategic research investments to improve decision-making, apart from the expected value of the investment (the EVPI), the impact of the research outcomes will be of major concern to the decision-maker: he or she would like to know whether the outcome of additional research is going to increase or decrease health-care costs and effects, what the likelihood of such scenarios is, and what the likelihood is that the outcome of additional research is going to change current policy. The first question is answered exactly by the AEVPI as it represents the expected change in costs and effects of additional research relative to the currently preferred intervention. The second question can be answered by looking at the “direction of change” probabilities for each of the quadrants: in example 1, there is 31% probability (Q3 + Q4 = 4% + 27%; Table 2) that obtaining perfect information will result in a cost reduction, whereas in example 2 there is a 39% (Q1) probability that this will result in an increase in costs (Table 2). The third question is merely the sum of the probabilities of change for the three relevant quadrant directions (Q1, Q3, and Q4).

In example 3 (Fig. 4), intervention (1) is compared to an expensive intervention with a highly uncertain effect. Intervention (2) has expected costs of $5000 (SD $500) and expected effects of –6 QALYs (SD 5 QALYs). As a result of the high uncertainty of the effect outcome, intervention (2) can potentially be far more effective than intervention (1). The benefits of reducing the current decision uncertainty are expressed in an EVPI of $6078. This is more than twice the EVPI from example 1. Nevertheless, although the VOI for this situation is considerably higher, adopting intervention (2) results in an increase in treatment costs. This is expressed in the AEVPI\(_{\text{Cost}}\), which in this case equals $408 compared with $309 in example 1. Moreover, there is a high chance (90%) that the additional research will not change the current preferred policy at all. This poses a higher (political) investment risk. Note that at the same time the returns can also be substantially higher, which is reflected in the higher EVPI. Nevertheless, the EVPI estimates presume a neutral risk.
Table 1: Simulated data for illustration of the attributable expected value of perfect information (AEVP) calculation

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¹Cost effectiveness threshold (CET): $25,000 per QALY.
²Overall preferred intervention (OPI): Intervention (1), because E(NMB) intervention (1) > E(NMB) intervention (2).
³If (G = J) then (E > B) then (E > D) then Q1 else Q4 else IF (D > A) then Q1 else Q4 else IF (B > C) else Q4. Blank.

In this table, calculation of the AEVP is illustrated for 20 random samples taken from two interventions with normally distributed costs and effects. Intervention (1) has mean costs of $1,000 (SD $400) and a mean effect of 0.2 QALYs (SD 0.3 QALYs). Intervention (2) has mean costs of $900 (SD $1000) and a mean effect of 0.1 QALYs (SD 0.2 QALYs). Based on the simulated costs (columns A and D) and effects (columns B and E), the NMB is calculated for each sample (columns C and F). The intervention with the highest average NMB (sample average of columns C and F) is the overall preferred intervention, which in this case is intervention (1) ($\$1025 > $1023). The AEVP is calculated using the preferred intervention per sample (columns H through K) and subtracting the overall preferred intervention outcomes (OPI, in this case the sample average of interventions (1), columns A through C). The results are given in columns L through N: the average of column L is the attributable EVPI cost (AEVPI), the average of column M is the attributable EVPI effect (AEVPIEffect), and the average of column N equals the total EVPI.

In column P, the direction of change (DOC) is given. In cases where the alternative intervention is preferred, the quadrant number indicates whether this intervention is going to be more costly and more effective (Q1), more costly but less effective (Q2), less costly and less effective (Q3), or less costly and more effective (Q4). In the "sample average" row, per quadrant the probability of occurrence is given. The sample average of the preferred intervention value is the estimated probability that the currently preferred intervention will change after obtaining perfect information on the intervention outcomes. This probability equals the sum of the direction of change probabilities per quadrant.
Figure 2: Expected value of perfect information (EVPI) and attributable EVPIs (AEVPIS) of example 1. Please note that minus the AEVPICost is shown so that the sum of the AEVPIS lines equals the (total) EVPI.

Figure 3: Attributable expected value of perfect information (AEVPIS) example 2. Average outcome and 95% confidence contours of intervention (1) (P1) with normally distributed costs $1000 (SD $600) and effects 0.2 quality-adjusted life-years (QALYs) (SD 0.3 QALYs), and intervention (2) (P2) with normally distributed costs $2900 (SD $1000) and effects 0.2 QALYs (SD 0.2 QALYs). The EVPI for this decision problem is $2755; the AEVPICost and AEVPIS are $734 and 0.140 QALYs, respectively.
attitude which might not at all be the risk attitude of the decision-maker. Both the impact on treatment costs and probability of policy change are important factors a decision-maker would like to take into consideration when comparing VOI outcomes.

**Discussion**

There are various other types of VOI analyses available in addition to the EVPI analysis as described in this article [6,10]. An example is the “expected value of partial perfect information” (EVPPI) [11]. Here, not the benefit from eliminating uncertainty in all model parameters is obtained, but of that of a particular parameter or a set of parameters. Another measure is the analysis of the EVSI [12]. In an EVSI analysis, a more realistic scenario for obtaining additional information (e.g., by performing a clinical trial) is defined and gains on improved decision-making are quantified. The outcomes of all current VOI analyses are hampered by the same limitations as described in this article. Fortunately, as the concept of calculating AVOI applies to the way results are presented and not to the way they are obtained, it can be applied to any VOI analysis. Often, VOI results are presented as a function of the CET (in case of EVPI or EVPPI), or as a function of the size of an additional randomized trial (in case of EVSI). This allows the decision-maker to analyze the sensitivity of the VOI. Any of these standard VOI results can easily be extended with AVOI results. As an example, Figure 2 provides attributable cost and effect values as a function of the CET. VOI analyses are generally performed by Monte Carlo simulations. Estimating the AVOI is as straightforward (or challenging) as estimating any of the existing VOI measures. Nevertheless, as both costs and effects are required for calculation of the NMB, which in turn is required to determine the preferred intervention, it is merely a matter of collecting the correct samples to enable calculation of the AVOI. This can be

![Figure 2](https://example.com/figure2.png)

**Figure 2** Attributable expected value of partial perfect information (EVPPI) example 3. Average outcome and 95% confidence contours of intervention (1) \((P_1)\) with normally distributed costs and effects of $1000 (SD $600) and 0.2 quality-adjusted life-years (QALYs) (SD 0.3 QALYs) and intervention (2) \((P_2)\) with normally distributed costs $5000 (SD $5000) and effects –6 QALYs (SD 5 QALYs). The EVPPI for this decision problem is $6079; the AEVPICost and AEVPIEffect are $408 and 0.259 QALYs, respectively.

**Table 2** Summary of characteristics and outcomes of all examples

<table>
<thead>
<tr>
<th>Description</th>
<th>Outcome of Intervention (2)*</th>
<th>Average (SD)</th>
<th>AEVPICost</th>
<th>AEVPIEffect</th>
<th>AEVPIDirection of change</th>
<th>Probability of change of preferred intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example 1</td>
<td>Cost ($) Effect (QALY)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Example 2</td>
<td>400 (1000) 0.1 (0.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Example 3</td>
<td>2900 (1000) 0.2 (0.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Example 4</td>
<td>5000 (500) –6.0 (5.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The average cost of intervention (1) is $1000 (SD $600), and the average effect is 0.2 QALYs (SD 0.3 QALYs).
†The AEVPIDirection of change is the product of the AEVPICost and the CET (25,000 per QALY).
‡Direction of change probabilities indicate the probability that the alternative intervention will either increase costs (Q1 and Q2), decrease costs (Q3 and Q4), increase effects (Q1 and Q4), or decrease effects (Q2 and Q3).
done with virtually no computational overhead to any of the existing procedures.

The AVOI provides a means to add relevant information to the current VOI, by providing the decision-maker with insight into the expected outcome of additional research in terms of changes in costs and effects of future interventions. In addition, the probability of change in any particular direction can be provided (e.g., the likelihood that costs and effects will increase [or decrease] as a result of the outcomes of additional research). Also, it allows assessment of the likelihood that the additional research will result in a change in current policy with respect to the preferred intervention. This additional information can be decisive when a selection has to be made between multiple research projects. The advantages of the AVOI in combination with the limited computational overhead required lead us to strongly recommend AVOI as a general extension to the existing presentation of VOI results.

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Supporting information for this article can be found at: http://www.ispor.org/publications/value/ViHsupplementary.asp

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