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A review of web-based tools for value of information analysis

Short title: value of information analysis tools

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Abstract

Value of information analysis (VOI) is a decision-theoretic approach that is used to inform reimbursement decisions, optimise trial design and set research priorities. The application of VOI analysis for informing policy decisions in practice has been limited due, in part, to the perceived complexity associated with the calculation of VOI measures. Recent efforts have resulted in the development of efficient methods to estimate VOI measures and the development of user-friendly web-based tools to facilitate VOI calculations. We review the existing web-based tools including Sheffield Accelerated Value of Information (SAVI), the web interface to the BCEA (Bayesian Cost-Effectiveness Analysis) R package (BCEAweb), Rapid Assessment of Need for Evidence (RANE), and Value of Information for Cardiovascular Trials and Other Comparative Research (VICTOR). We describe what each tool is designed to do, the inputs they require, and the outputs they produce. Finally, we discuss how tools for VOI calculations might be improved in the future to facilitate the use of VOI analysis in practice.

Key Points for Decision Makers

- The web-based tools reviewed provide user friendly and free to use platforms to rapidly calculate VOI measures.
- The choice among these tools should depend on what health economic context the VOI analysis is being used in, and whether it is feasible to develop a full decision-analytic model for the required context within time and resource constraints.
- Effective communication of the value of VOI analysis and continuous capacity building efforts will enhance the utilisation of VOI analysis and its tools in practice.

1. Introduction

Value of information (VOI) analysis provides an analytic framework to assess the value of research, based on the notion that generating new information would reduce decision uncertainty and optimise the expected payoffs associated with a decision [1]. The expected value of research can then be compared with its costs to inform important decisions including reimbursement decisions (e.g., coverage conditional on collecting further evidence), efficient study design, and research prioritisation [2-5].

The three VOI measures that are used to inform reimbursement and research decisions are the expected value of perfect information (EVPI), the expected value of perfect parameter (or partial perfect) information (EVPPI), and the expected value of sample information (EVSI). The EVPI represents the value of research that resolves all uncertainty in all input parameters whereas the EVPPI measures the value of research that resolves all uncertainty in a single parameter or a subset of parameters, and hence informs the focus of research (i.e., which parameters to target in further research) [1, 6-8]. The EVSI represents the value of a specific research study design that will reduce (but not eliminate) uncertainty about one or more model parameters.

All three VOI measures are typically calculated in terms of individual-level value, but when expressed on a population level by multiplying by the size of the population affected by the decision, they can be compared to the costs of additional research. Importantly, EVPI and EVPPI measure the expected value of research that would provide *perfect* information on considered parameters (i.e., that would eliminate all decision uncertainty), but obtaining perfect information requires a perfect study with infinite sample size, which is not feasible in practice. Nevertheless, the (population-level) EVPI and EVPPI describe the maximum expected value of research (i.e., the expected upper bound) which can be used to screen research proposals [1, 6-8]. For instance, when the EVPI appears to be small compared with research costs, additional research would not be worthwhile. However, to establish a *sufficient* condition to decide whether additional research is worthwhile, expected research costs should be compared with the EVSI, which represents the expected value of a research study with a specific sample size and design in reducing uncertainty [1, 6-8].

The calculation of VOI measures typically requires conducting a cost-effectiveness analysis using decision analytic modelling, and characterisation of decision uncertainty by expressing input parameter uncertainty in terms of probability distributions. Given a probabilistic model of this kind, the EVPI can be computed straightforwardly using spreadsheet software [9]. Calculations of the EVPPI and EVSI are more challenging. EVPPI has only become generally practicable since the recent development of efficient computational methods and tools to implement them, and EVSI still requires advanced analytical and simulation skills [10, 11]. Thus the calculation of VOI measures can be a challenging task for analysts and a resource exhausting exercise for organisations that lack the capacity to conduct such complex analyses.

To promote and enhance the application of VOI analysis, VOI researchers from two professional groups, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) VOI Task Force and the Collaborative Network for Value of Information (ConVOI) [1, 6, 12], have developed best practice guidelines for VOI analysis and developed web-based tools based on efficient VOI methods to facilitate the calculation of VOI measures [1, 6, 12]. These tools are based on different methods of modelling and VOI calculation, and are used to address different types of decisions. They also vary in their inputs and outputs as well as in the required skills to use them. Thus, users may need guidance about which tool to use and how best to use each tool to inform decision making. The aim of this paper, therefore, is to review existing web-based VOI tools and provide expert advice about what each tool is designed to do, the inputs they require, the outputs they produce, and when to use each of these tools.

2. Approach

Given the limited number of researchers who work in the field of VOI research, we identified the web-based tools from the websites of professional and research groups known to us in the ConVOI consortium [12]. We concentrate on web-based tools since these are the most accessible to users, and require no programming skills; however, some more specialised tools are mentioned in our final Discussion.

We reviewed publicly available information on the websites hosting these tools and combined this information with supporting methodological papers, personal communications with their developers, and the ConVOI consortium's expert opinion [10, 11, 13]. We provide a description of each tool, its purpose and methodology as well as the input parameters it requires and the VOI measures calculated. In addition, we provide recommendations about when to use each tool. Finally, we discuss how tools for VOI calculations might be developed in the future to facilitate the use of VOI analysis in practice.

3. The web-based VOI tools

Currently available free web-based VOI tools are 1) Sheffield Accelerated Value of Information (SAVI), 2) the web interface to the BCEA (Bayesian Cost-Effectiveness Analysis) R package (BCEAweb), 3) Rapid Assessment of Need for Evidence (RANE), and 4) Value of Information for Cardiovascular Trials and Other Comparative Research (VICTOR). These can be categorised into tools that are based on outputs from a full decision-analytic model supplied by the user, and tools that use built-in minimal models where the only uncertainties considered are about primary and secondary intervention effects. Table 1 summarises the web-based tools in terms of their purpose, need for decision-analytic modelling, inputs and outputs.

3.1 Tools based on full decision-analytic modelling

These tools require the development of a decision-analytic model and the results of a probabilistic analysis (PA), which are obtained by assigning probability distributions to input parameters, randomly sampling from those distributions, and evaluating the corresponding decision model outputs.

Sheffield Accelerated Value of Information (SAVI)

This tool was developed at the University of Sheffield's School of Health and Related Research. It is based on the regression-based method for approximating EVPPI calculation and programmed as an R-Shiny Server application http://savi.shef.ac.uk/SAVI/ [13]. In addition to uploading the PA results, the user is asked to provide information required to convert the individual-level expected outcomes produced by the model to population-level VOI measures, including effectiveness (e.g., quality-adjusted life years (QALYs) or life years) and cost measures and units, the willingness-to-pay threshold, the size of the population that will be affected by the decision each year (i.e., annual prevalence), and the time horizon of the decision (i.e., number of years that the decision is relevant).

SAVI estimates the individual-level EVPI in monetary terms, per jurisdiction per year, and over the decision relevance horizon, as well as the EVPPI for single parameters and groups of parameters. While not fully supported by SAVI, and given the similarity in calculating EVSI and EVPPI using the regression-based approach, the tool can be used to calculate EVSI by augmenting PA results with simulated data from the proposed study design of interest [14]. An additional feature of SAVI is the financial risk analysis component which estimates Payer Strategy-Specific Burden (PSB) and Payer Uncertainty Burden (PUB) [15]. The PSB represents the risk of choosing an alternative that is not the most cost-effective option. The PUB is equivalent to the EVPI as it indicates the risk of making the decision with current evidence, relative to making the decision with perfect evidence [15]. SAVI produces a report in pdf, html or docx format that summarises the results of the VOI analysis in text, tables and graphs.

The web interface to the BCEA (Bayesian Cost-Effectiveness Analysis) R package (BCEAweb)

This tool provides a web interface for the BCEA (Bayesian Cost-effectiveness Analysis) R package, implemented as an R-Shiny app https://egon.stats.ucl.ac.uk/projects/BCEAweb/ [16, 17]. Like SAVI, it is designed to post-process the results of a PA, which can be uploaded using many different formats, including CSV files and CODA format files (e.g., OpenBUGS or JAGS). The user is also asked to include a plausible range of willingness-to-pay thresholds. The tool estimates EVPI and EVPPI in monetary terms, and, like SAVI can be used to estimate EVSI if simulated datasets are

uploaded as parameter samples. The results are summarised in a report that includes useful graphs such as the cost-effectiveness acceptability curves, cost-effectiveness acceptability frontier, and the "info-rank" plot, which is useful to assess how parameters contribute to the uncertainty in the model by ordering them in decreasing order of the ratio of the single-parameter EVPPI to the EVPI for a given willingness-to-pay threshold.

3.2 Tools based on built-in minimal models

In a full probabilistic decision-analytic model, all potential sources of uncertainty that might affect the decision are parameterised and characterised by probability distributions. However, often, only a limited number of uncertain parameters will be expected to affect the decision, most commonly those related to intervention effectiveness. This has motivated "minimal modelling" approaches to VOI calculations [18-20], in which the only uncertainty described is about the primary intervention effects, and these effects can be related straightforwardly to the outcome used for decision making (e.g., QALYs). The results thus describe the expected value of information about those intervention effects alone.

Rapid Assessment of Need for Evidence (RANE)

RANE was developed at the Centre for Health Economics, University of York and programmed using R-Shiny https://shiny.york.ac.uk/rane/ [21]. The purpose of this tool is to calculate the value of research proposals to inform research funding and prioritisation decisions. It assumes that research can have two kinds of value: 1) obtaining new primary data (e.g., a clinical trial) to add to the current evidence base, or 2) highlighting existing published evidence (e.g., through systematic review) that the currently implemented health policy does not take into account. In either case, the research results in additional evidence, about the effectiveness of the interventions of interest that could influence implementation in practice and improve patient outcomes [21]. Importantly, RANE does not require a decision-analytic model. Instead, it requires a point estimate of intervention effectiveness on a primary outcome measure (e.g., relative effectiveness measure) and an associated measure of uncertainty (e.g., confidence interval) around that estimate, which can come from a systematic review and meta-analysis, expert elicitation, meta-epidemiological evidence, or a combination of these sources [20, 21].

Depending on the type of the primary outcome (e.g., progression free survival), other inputs include treatment and disease related costs, health states, health utility associated with the health states, and the time horizon. To capture the value of research in improving implementation in practice, the tool requires information about the baseline uptake rates of both the intervention and the comparator. Additionally, the tool requires information about the intended research study in terms of its type (e.g., randomised control trial, pilot study), the expected duration of the study, the time over which the generated evidence would be available and useful, the disease incidence, the cost of the study to the funder, and the discount rate. The VOI estimations reported by RANE only relate to information about the intervention effects, since uncertainty about any other parameters is not modelled. Thus the result could be described either as the EVPI under this minimal modelling approach, or the EVPPI related to the intervention effect parameters. In situations where there are a number of other important aspects of outcome that are not captured in the primary outcome (e.g., adverse events, quality of life impact or resource implications), a minimum clinical difference (MCD) in effectiveness in the primary outcome may be specified in order to capture these additional considerations. For example, a certain MCD in effectiveness in the primary outcome may need to be detected in a new research study before there is confidence that health outcomes will be improved. The EVSI is not currently calculated, thus the research value estimated by the tool represents the

expected upper bound for the value of research on the intervention, which is still useful to rapidly screen and exclude proposals with low expected value. The value of research calculated by RANE can be expressed in clinical terms (e.g., outcome gained/avoided) or using QALYs gained.

Value of Information for Cardiovascular Trials and Other Comparative Research (VICTOR)

VICTOR was developed based on collaborative work between The CHOICE Institute and the Department of Cardiology at the University of Washington, and uses the R-Shiny framework https://uwchoice.shinyapps.io/victor/ [22]. The tool aims to help researchers estimate the potential value of their cardiovascular disease studies. The minimal model in VICTOR is a simple Markov model that follows patients until they experience certain cardiovascular endpoints (e.g., stroke, myocardial infarction) [18, 23]. At that point, life expectancy is calculated based on patient characteristics (e.g., age and gender) and the type of event using validated life-tables. The tool estimates the EVPI and EVSI, expressed in terms of life-years gained at a population level or a per-patient level. Similarly to RANE, the only uncertainties that are modelled are related to the intervention effects. In VICTOR these uncertainties can either be placed on the relative effect of two interventions on the primary outcome, or on the (absolute) rates of the outcome under each of the interventions.

Inputs include relevant demographic information such as gender, age and history of cardiovascular disease as well as primary and secondary cardiovascular endpoints, target population size, treatment effectiveness duration, treatment utilisation rate, decision-making considerations, study duration and sample size, and discount rate. For EVSI calculation, additional inputs are required including the length of the proposed trial, the sample size in each arm, and a number of sample sizes to be evaluated. Of note, VICTOR allows for adjusting VOI estimates based on certain decision criteria [18, 23]. For instance, a decision to adopt an intervention would be made only if the new intervention is statistically more effective than the standard of care. VICTOR reports population and per-patient EVPI expressed in life years. It also produces EVSI tables and graphs showing population and individual-level EVSI estimates in years for different sample sizes.

4. When to use each tool

The four tools are essentially distinguished by the form of decision-analytic model that they are designed to work with. SAVI and BCEAweb work with models of any level of generality, and require a probabilistic decision-analytic model to be developed separately by the user. However in RANE and VICTOR, a minimal model is encoded in the tool itself, and the only uncertainties modelled relate to primary treatment effects. The choice among these tools, therefore, should depend on what health economic context the VOI analysis is being used in: whether the model assumed by the tool accurately represents the decision problem and whether we only wish to estimate the value of research on intervention effects, and if not, whether it is feasible to develop a full decision-analytic model for the required context within time and resource constraints.

SAVI and BCEAweb are practical and efficient tools to estimate VOI measures when the results of a PA from a decision-analytic model are available. The risk analysis component in SAVI makes it appealing to Health Technology Assessment (HTA) settings where conducting VOI might be useful to inform coverage with evidence development decisions (e.g., managed entry agreement) [4, 24, 25]. However, conducting decision modelling may not be practical or feasible for many organisations due to lack of the required skills, where probabilistic analysis is not an essential component of reimbursement submissions (e.g.,

Australia), or where economic evaluations are not recommended to inform decision making (e.g., USA). Under such constraints, tools with built-in minimal models, such as RANE and VICTOR, may provide a practical alternative to full decision-analytic modelling. The advantage of "minimal modelling" lies in the simplification of the modelling exercise to rapidly calculate VOI measures based on a limited number of inputs, which may help funding bodies prospectively assess the value of research proposals using the inputs provided in research funding applications. Nevertheless, tools based on "minimal modelling" should be used with caution, because a simple packaged model may not be suitable for the required context, and may neglect aspects of the clinical and economic processes that might affect the required decisions and value of further information [2].

While SAVI and BCEAweb have the advantage of estimating both EVPI and EVPPI, EVSI estimation is not fully supported by either of the tools in their current form. However, RANE and VICTOR only estimate the EVPI about the principal intervention effectiveness parameters, which is sufficient if other potential sources of decision uncertainty are deemed to be negligible. Even if EVSI cannot be calculated, any of these tools may still be used to screen submissions. If the EVPI is lower than the cost of research, then the value of additional research is negligible (i.e., current evidence is sufficient), and thus a decision can be made to adopt or reject a technology based on existing evidence [4]. Furthermore, EVPPI helps to identify the parameters that are important in driving the decision uncertainty. However, when EVPI and EVPPI estimates suggest additional research appears to be worthwhile, the decision to conduct that research cannot be confirmed without estimating EVSI and comparing EVSI estimates with research costs, including the opportunity cost of delaying implementation as well as sunk costs that cannot be recovered if the technology turned out to be less effective that it was initially thought [4, 26]. Although VICTOR estimates EVSI, this estimation is for a particular parameter related to the relative effectiveness of the intervention and only within the cardiovascular disease context.

5. Future directions

The four tools reviewed provide user friendly and free to use web-based platforms to rapidly calculate VOI measures. However, and despite the highlighted advantages of the tools, there are some considerations that should be addressed to improve their utilisation in practice.

A major limitation is the lack of modules to readily estimate EVSI in most of the tools. EVSI estimates the value of a study of a specific design and sample size, thus if the EVSI is greater than the expected cost of the study, then the study is judged to be of value. SAVI and BCEAweb, on the other hand, can be used to calculate EVSI by simulating potential data sets to generate summary statistic for specific data collection exercises; however, simulating potential data requires statistical skills. Recent research has compared the accuracy and efficiency of different methods for calculating EVSI [11]. While there is currently no web-based tool for these methods, they can all be implemented in R, and the skills required for users to apply them are discussed in a recent paper by Kunst *et al* [10]. As part of the ConVOI initiative, work is ongoing to develop an easily-usable R package [27] to implement all practicable methods of calculating EVSI (and EVPPI) given samples from a probabilistic decision-analytic model, which might also be used as the "engine" for a web-based user interface.

Despite the rigorous methodologies behind these tools, their application in practice has yet to be tested in terms of acceptability, fit for purpose and practicality by end users. This is of a particular concern to funding bodies who have large numbers of HTA submissions or research proposals to assess within a short time. One possibility is to prioritise which proposals

would require VOI analysis based on certain criteria (e.g., when a high budget is required) [2, 28]. Moreover, there are other decision criteria that are considered together with value for money of an intervention or a research study. These may include equity, feasibility, relevance to organisational strategic goals and benefits beyond health gains [2, 29, 30]. It would be interesting to study the impact of these considerations on VOI estimates and to develop approaches to aggregate multiple elements of research benefits. This highlights the importance of stakeholders' engagement in the development and implementation of VOI tools. Early and effective engagement would ensure that the tool meet the needs and expectations of end users in terms of its purpose, data availability and the skill mix required to use the tools. An excellent example was the development of RANE firstly through a partnership between the University of York and the Patient Centred Outcome Research Institute (PCORI) in the US [20] and subsequently by the National Institute for Health Research (NIHR) Evaluation, Trials and Studies Coordinating Centre (NETSCC) in the UK.

Intuitively, stakeholders' needs and their capacity to conduct VOI analyses vary significantly within the one country and across different jurisdictions, which may limit the utilisation of a tool developed specifically for a particular organisation or a specific disease (e.g., cardiology). Developing a generic tool that can provide comprehensive VOI analysis solutions for all purposes and settings would be ideal, however, this task would be complex and resource intensive.

Effective communication of the value of VOI analysis and continuous capacity building within the organisations involved will enhance the utilisation of VOI analysis and its tools in practice. Importantly, the users of these tools should be able to interpret the results and use them to inform the decision problems under considerations. ISPOR VOI best practice guidelines will be instrumental in providing the necessary recommendations to guide the planning, conduct, analysis, reporting and interpretation of VOI analysis [1, 6]. ConVOI members will continue to develop and refine the VOI tools to better meet the expectations of end users. Further workshops, courses and tutorials may be warranted to build the skills required to perform VOI analysis using the web-based tools. Future research may focus on understanding the barriers and facilitators for VOI tools utilisation in practice as well as identifying aspects to improve the existing tools.

We have only reviewed web-based tools for VOI calculation, since they are easily and freely accessible and require no programming skills – however we note there are other more specialised tools available that implement VOI methods. For example, SAVI and BCEAweb are also available in the form of R packages, and some spreadsheet-based tools have been developed for VOI calculations in specific decision-making contexts [31], or for tutorial purposes [32].

Declarations

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Conflicts of interest/Competing interests

MS, CJ, CR were involved in the development of some of the tools reviewed. HT, NK and SB have no conflict of interest.

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Authors' contributions

HT Conceptualised and drafted the manuscript. All authors critically revised the manuscript and approved the final version.

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Table 1: Summary of the four VOI web-based tools

VOI tool	Main purpose	Full decision-analytic model required	Key Inputs	VOI measures	Other outputs
SAVI	General assessment of VOI measures, focus on HTA	Yes	PA results, effectiveness and cost measures and units, WTP, population size and time horizon	EVPI, EVPPI	CEAC, INB, PSB,PUB, and a summary report of results
RANE	Rapid assessment of the value of research proposals	No	Type of research, research duration and cost, type of primary endpoint and the level of uncertainty around that endpoint, WTP, population size and time horizon, uptake rate of interventions	EVPI	Expected benefits from improving implementation in practice
BCEAweb	General assessment of VOI measures	Yes	PA results, effectiveness and cost measures and units, WTP, population size and time horizon	EVPI, EVPPI	CEAC, CEAF, and the "info-rank" plot, and a summary report of results
VICTOR	Assessment of the value of research proposals in cardiovascular studies	No	Demographic information, primary and secondary endpoints, duration of the study and sample size, treatment duration and utilisation rate, and population size.	EVPI, EVSI	Survival curves, EVSI over different sample sizes tables and graphs

Abbreviations: CEAC: cost-effectiveness acceptability curve; CEAF: cost-effectiveness acceptability frontier; HTA: health technology assessment; INB: incremental net benefit; PA: probabilistic analysis; PSB: payer strategy-specific burden; PUB: payer uncertainty burden; WTP: willingness-to-pay threshold;