Value of Information Analysis in Health Care: A Review of Principles and Applications

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Value of Information Analysis in Health Care: A Review of Principles and Applications

Abstract

Background

Economic evaluations are increasingly utilized to inform decisions in health care; however, decisions remain uncertain when they are not based on adequate evidence. Value of information (VOI) analysis has been proposed as a systematic approach to measure decision uncertainty and assess whether there is sufficient evidence to support new technologies.

Scope

The objective of this paper is to review the principles and applications of VOI analysis in health care. Relevant databases were systematically searched to identify VOI articles. The findings from the selected articles were summarized and narratively presented.

Findings

Various VOI methods have been developed and applied to inform decision making, optimally designing research studies and setting research priorities. However, the application of this approach in health care remains limited due to technical and policy challenges.

Conclusion

There is a need to create more awareness about VOI analysis, simplify its current methods, and align them with the needs of decision making organizations.

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Introduction

Comparative effectiveness research has been proposed as a potential avenue to identify, evaluate, and provide effective, safe, and cost-effective health care on the basis of informed and evidence-based decisions.(1) When comparing alternative health care options, it is essential to identify and combine the best available evidence on treatment effects, health-related preferences (utilities), resource use, and costs.(2) Nevertheless, the evidence could be absent or uncertain due to the limitations and weaknesses of the available studies. A cost-effectiveness analysis that is based on such evidence is uncertain, and thus, any decision based on this analysis will also be uncertain.(3) Decision uncertainty is associated with risk because making the wrong decision could lead to costly consequences for the health care system (e.g., adopting suboptimal treatment). Acquiring additional information could reduce uncertainty and better inform decisions; however, there is a cost for obtaining further evidence in terms of the direct costs of conducting research and the opportunity cost of delaying the decision awaiting research results.(3, 4) In addition, under limited budgets, the money spent on a specific research study could be spent on health care or on other competing research proposals. Therefore, it is recommended to assess the need and value of additional research before making decisions.(5, 6)

Value of information analysis has been proposed to aid decision makers decide simultaneously on the adoption of new technologies and the need for further research. Various value of information methods have been developed and successfully applied to

inform whether there is sufficient evidence to support new technologies, optimally designing research studies and setting research priorities.(7, 8)

The majority of the published papers on value of information analysis are methodological.(7) Even in the applied papers, the topic is often presented with complexity rendering this approach difficult to grasp by non-specialist. Thus, there is a need to present the principles and advantages of value of information analysis to decision makers, researchers, and practitioners in a succinct but comprehensive manner. The objective of this paper is to review value of information principles and applications in health care.

Scope

The first section of this paper describes the principles of value of information analysis, and the second section reviews the applications of value of information in health care. The general approach is to identify the relevant literature to inform this review searching various databases including PubMed, Medline, CINAHL and the National Health Service Economic Evaluation Database for value of information articles published from January 2003 to January 2013. Search terms included: ‘value of information’, ‘value of perfect information’, ‘value of sampling information’, and ‘value of perfect parameter information’. These terms were searched in combination with the terms ‘decision making’, ‘trial design’ and ‘research prioritization’. A narrative approach is used to summarize and present the principles and applications of value of information from the reviewed articles.

1. Principles of Value of Information Analysis

Value of information analysis provides an analytic framework to quantitatively estimate the value of acquiring additional evidence to inform a decision problem. It is based on the

notion that information is valuable because it reduces the expected cost of making the wrong decisions under uncertainty.(5, 6) By measuring the expected benefits of additional evidence and comparing this with the expected costs of further research, the value of information approach helps decision makers answer the following five related questions:(8, 9)

1. Is additional research required? And if yes,
2. What type of research?
3. Do the benefits of research exceed the costs?
4. What is the optimal research study design?
5. What priority should this research study take?

1.1 Is additional research required?

To know whether additional research is required, it is essential to consider the expected cost of the consequences of making a wrong decision (i.e., the cost of uncertainty).(3) High expected cost of uncertainty indicates a need for acquiring further information before making a decision. The expected cost of uncertainty is determined by two factors: 1) the probability that a decision is wrong, and 2) the consequences of this potentially wrong decision.(9)

To explain how the cost of uncertainty is estimated, a simplified hypothetical example is presented for two treatment interventions (A and B) modeled in a cost-effectiveness analysis. The uncertainty in the results of the cost-effectiveness analysis is characterized by presenting the expected net benefit estimates (i.e., effects measured in monetary terms minus costs) for each intervention. In this example, the model is calculated five times to reflect various possible values of the model parameters (Table 1). Because the expected average net benefit for intervention B (\$1,200) is higher than for A (\$1,000), selecting intervention B would be the best decision. However, this decision is imperfect as there is a 40% probability that a

wrong decision is made; in two out of five scenarios treatment A is cost effective. The consequence of this wrong decision is the opportunity loss (i.e., benefit forgone) from choosing treatment B when treatment A was the preferred intervention. This opportunity loss is calculated by taking the difference between the net benefits of the two interventions in each scenario when A was preferred. The average opportunity loss across all scenarios is the expected cost of uncertainty of the decision for adopting treatment B, which is \$40 per patient in this example. Equivalently, if we knew all parameters with absolute certainty (i.e., we have perfect information), we would choose the intervention with the maximum net benefit in each scenario. Averaging the maximum values across all scenarios gives the expected benefit of a decision made with perfect information, which is \$1,240. The difference between the expected benefit of a decision made with perfect information and a decision made without perfect information ($\$1,240 - \$1,200 = \$40$ per patient) is the expected value of perfect information (EVPI) which is also the expected cost of uncertainty.(10)

<<TABLE 1 GOES HERE>>

The EVPI calculated above is an average estimate (i.e., per patient EVPI). Multiplying per-patient EVPI by the population of patients expected to benefit from the evaluated intervention over a period of time gives the population EVPI which represents the maximum potential value (i.e., upper bound) of additional research.(8, 9) If the population EVPI appears to exceed the cost of additional research study, then this study is potentially worthwhile and further assessment is required to inform its optimal design.(9, 11) Nevertheless, it has been argued that population EVPI is neither necessary nor sufficient to inform whether additional research is worthwhile because it is impossible to estimate the expected cost of research without knowing the specific research study design (e.g., sample size, follow-up time).(8) However, calculating population EVPI is relatively simple and

considered a continuation step to uncertainty assessment in cost-effectiveness analyses. When the population EVPI approaches zero it is unlikely that the value of additional research will exceed its cost and there will be no need to undertake further value of information analyses.(12)

1.2 What type of research?

If further research appears potentially worthwhile based on the population EVPI, it would be useful to identify the particular aspects of a decision problem that are worth studying to resolve the uncertainty surrounding them.(11) This could be achieved by estimating the expected value of information for certain input parameters in a given economic evaluation, often referred to as the partial EVPI or the expected value of perfect parameter information (EVPPI).(3) EVPPI is defined as the difference between the expected value of a decision made with perfect information on the selected parameters and the decision made based on current information.(11) EVPPI serves as a measure of the sensitivity of the economic evaluation to the uncertainty in its different input parameters.(3, 11) A parameter with a higher EVPPI is more uncertain and further research can be designed and focused to get more precise estimate of its value. Importantly, the nature of the uncertain parameter(s) would inform the type and possibly the cost of the additional research study needed (e.g. randomized controlled or observational).(3, 11)

1.3 Do the benefits of research exceed the costs?

When the benefits of additional research study in reducing decision uncertainty exceeds its total cost, then this study is worthwhile. EVPI and EVPPI measure the expected value of additional research providing perfect information to resolve uncertainty of all parameters or specific parameters.(10) However, acquiring perfect information requires a

very large research sample (i.e., infinite sample size) which is not practical. In reality, it is only possible to reduce uncertainty with additional information from a research study of a finite sample size.⁽⁵⁾ The expected value of sample information (EVSI) estimates the expected value of reducing the uncertainty by a given research study with a specific sample size within a particular study design.⁽⁸⁾ This can be calculated for all effect and cost parameters (i.e., total EVSI) or for the parameter(s) of interest (i.e., partial EVSI).⁽¹³⁾ Population EVSI is calculated by multiplying the per-patient EVSI by the size of the population to whom information from the trial is valuable.⁽⁸⁾

The expected total cost of a research study includes three components: 1) fixed cost (e.g., set-up cost, salaries), 2) variable cost per patient, and 3) an opportunity cost for those patients who receive the inferior intervention while the study is underway.⁽⁶⁾ The total cost commonly takes a societal perspective; however, this cost may also be from the perspective of the sponsor of the study. The difference between the population EVSI for a specific study design and its expected total cost is the expected net benefit of sampling (ENBS).⁽⁸⁾ A positive ENBS indicates that the research study is worthwhile. Conversely, when the ENBS is negative, it would be irrational to conduct further research because the expected costs of the study exceed its expected benefits, and in this case, the current available evidence is sufficient for decision making.⁽¹⁴⁾ The EVSI and the ENBS are the preferred measures of value of information because they are sufficient to inform whether a specific research study is potentially worthwhile.⁽⁸⁾

1.4 What is the optimal research study design?

The sample sizes of clinical trials are usually calculated based on type I and II error, and the minimum clinically important difference.⁽¹⁵⁾ The value of information framework

provides an alternative to the standard hypothesis testing approach which relies on arbitrary chosen error probabilities where type I and type II error receive the same weight (e.g., 5% and 20% respectively) regardless of the consequences of making an error.(10, 16) Figure 1 shows the population EVSI across a number of sample sizes for a future research study. As the sample size increases and more uncertainty resolved the calculated population EVSI converges to the population EVPI (i.e., upper bound). Deducting the expected total cost from the EVSI results in the ENBS curve which, in this example, is positive for a wide range of sample sizes; however, the ENBS is at maximum when the sample size is 250 patients in each arm which represents the optimal sample size.

<<FIGURE 1 GOES HERE>>

Beyond sample size determination, value of information analysis can optimize additional aspects of research design such as possible comparator arms and alternative follow-up periods.(8, 17) More uncertainty is expected to resolve with longer follow-up and more comparator arms albeit with additional research costs. The preferred trial design would be the one that maximizes the ENBS.(8)

1.5 What priority should this research study take?

Typically, decisions to fund and prioritize research proposals have been subjectively made based on the opinions, judgments and consensus among experts on a research panel evaluating the scientific merit and relevance of the proposals.(18) However, different objective approaches have been proposed and implemented to prioritize research projects such as the burden of disease and the ‘payback’ approach.(18, 19) In the burden of the disease, the higher the cost of a disease the greater the need for research; however, this does not take into consideration the expected incremental costs and returns from the additional research.(8, 18) Moreover, the burden of the disease approach might undermine investment in

rare diseases as it focuses the decision maker's attention on common diseases where there is usually a high illness cost. In the 'payback' approach, however, the costs and benefits from conducting and implementing research are evaluated and compared.(8, 18) Under this approach, a research project is worthwhile if its benefits outweigh the expected costs.(18) Nevertheless, the 'payback' requires the comparison of the costs and benefits of undertaking a predesigned research project, implicitly assuming that the proposed research has been optimally designed.(20) The value of information analysis has been proposed as an alternative quantitative approach to prioritize research studies.(8, 21) Under the value of information approach, competing research proposals are ranked according to their expected values whereby priority is given to the studies with the highest ENBS.(8) This is illustrated in a hypothetical example in Table 2 where five research proposals are being compared. Nevertheless, it has been argued that the proposal with the highest ENBS may not necessarily provide the highest return on investment (i.e., ENBS divided by the expected total cost of research).(8)

<<TABLE 2 GOES HERE>>

2. Value of Information Applications in Health Care

Value of information analysis is increasingly applied in health care to inform decisions, optimize trial design and prioritize research.(8) In a systematic review on the application of value of information in health technology assessment a total of 118 papers were identified of which 59 were applied.(7) The authors of this review observed a rapidly accumulating literature base on value of information from 1999 onwards for methodological papers and from 2005 onwards for applied papers.(7) Most of the identified applied articles estimated the EVPI and the EVPPI indicating that the majority of the studies used the value of information approach to estimate the maximum value of additional information to assess

whether further research is warranted.(7) However, limited number of applied papers reported the preferred value of information measures of EVSI (six articles) and ENBS (four articles).(7) Similar results were reported in a recent systematic review on value of information application in oncology where less than 10% of the identified articles reported the use of this approach to inform optimal trial design and research prioritization.(22)

2.1 Informing decisions

The most explicit use of value of information methods to inform decisions is by the National Institute for Health and Clinical Excellence (NICE) in England. Claxton and colleagues(9) have developed a value of information based framework for NICE to inform the following decision options:

1. Approve based on existing information.
2. Approval with research (i.e., Approve and ask for additional research)
3. Only in research (i.e., Delay approval and ask for additional research)
4. Reject based on existing information.

Generally, when the technology is cost-effective ‘approval with research’ would be appropriate if additional research is possible and worthwhile.(9) Conversely, if the technology is not cost-effective but additional research is worthwhile, ‘only in research’ would be the preferred option. Nevertheless, exceptions from this general rule would be appropriate depending on the presence of irrecoverable cost associated with the adoption of the new intervention (e.g., cost of training).(9) Thus, ‘only in research’ or even ‘reject based on existing information’ rather than ‘approval with research’ or ‘approve based on existing information’ may be appropriate even if research is possible when there are significant irrecoverable adoption costs.(9)

A recent study reviewed NICE technology appraisals with ‘only in research’ or ‘approval with research’ recommendations and examined the key considerations that led to those decisions.(23) In total, 29 final and 31 draft guidance documents included ‘only in research’ or ‘approval with research’ recommendations up to 2010. Overall, 86% of final guidance included ‘only in research’ recommendations. Of these, the majority was for technologies considered to be cost ineffective (83%) with 66% of the final guidance specified the need for further evidence on relative effectiveness.(23)

From the industry perspective, any change in the price of the intervention, such as through patient access schemes or price negotiations, will affect the key assessments, and possibly leading to a different decision.(9, 24) Subsequently, once the need for additional information and the size of irrecoverable costs are recognized, the threshold price that would lead to ‘adopt based on existing evidence’ rather than ‘only in research’ will always be lower than a single value-based price based on expected cost effectiveness alone.(9) Willan and Eckermann have proposed a framework to bring together the societal and industry perspectives, allowing for trade-offs between the value and cost of research and the price of the new intervention.(25) Under this framework, if the decision maker’s threshold price exceeds the sponsor’s (industry), then current evidence is sufficient since any price between the thresholds is acceptable to both. However, if the decision maker’s threshold price is lower than the company’s, then no price is acceptable to both and the company’s optimal strategy is to conduct additional research.(25)

2.2 Optimizing trial design

The use of the value of information methods in optimizing trial design remains limited and most applications have been restricted to the estimation of optimal sample size, and mainly in two-arm randomized trials.(14, 26, 27) For example, Koerkamp and colleagues applied value of information analysis to patient-level data from two randomized trials on intermittent claudication and magnetic resonance imaging (MRI) in acute knee trauma.(26, 28) The optimal study design for the treatment of intermittent claudication would involve a randomized controlled trial collecting data on the quality-adjusted life expectancy and additional admission costs for 525 patients per treatment arm.(26) For the MRI in acute knee trauma, three parameters were found responsible for most of the decision uncertainty: number of quality-adjusted life-years, cost of an overnight hospital stay, and friction costs.(28) A study in which data on these three parameters are gathered would have an optimal sample size of 3,500 patients per arm.(28) Soares *et al.* showed how value of information analysis informed the optimal future trial design on negative-pressure wound therapy for severe pressure ulcers.(29) In their study, a three-arm trial with one-year follow-up and a sample size of 497 patients (in each arm) was estimated to be the most efficient.(29)

2.3 Prioritizing research

In a survey prepared for the Agency for Healthcare Research and Quality (AHRQ), research prioritization approaches for 48 research-sponsoring organizations from the United States, United Kingdom, Australia, Germany, and Canada were identified and compared.(30) The results showed that only 31 (65%) organizations utilized specific priority-setting methods. The most explicit use of value of information and other quantitative methods was by NICE, where the assessment is usually performed by a network of academic centers under the umbrella of the National Institute for Health Research (NIHR) Health Technology Assessment program. (30) This is expected, because in the United Kingdom where research

is often commissioned on a tender basis, the application of value of information methods in identifying areas of value for funding bodies may be useful. On the other side, in settings where grant applicants have more active role in defining research questions (e.g., United States and Australia), it is suggested that more emphasis be placed on application of value of information methods by applicants in showing the connection of proposed trial designs to value of research and decision making.(8)

Recently, Carlson *et al.* have evaluated the feasibility and outcomes of incorporating value of information analysis into a stakeholder-driven research prioritization process within a program to prioritize comparative effectiveness research in cancer genomics.(31) The authors described how they convened an external group of stakeholders to identify three high-priority cancer genomics tests for further research and to rank these in order of priority for conducting further research.(31) These test included expression testing for platinum-based adjuvant therapy (ERCC) in resectable non-small cell lung cancer (NSCLC), epidermal growth factor receptor (EGFR) mutation testing for erlotinib maintenance therapy in advanced NSCLC and breast cancer tumor markers (BC markers) for detection of recurrence after primary breast cancer therapy.(31) The study demonstrated how providing the stakeholders with value of information estimates about the three tests resulted in participants changing their ranking of the tests from 1) ERCC1, 2) EGFR, 3) BC markers to 1) ERCC1, 2) BC markers, 3) EGFR.(31)

2.4 Challenges for value of information application

The wide adoption of value of information methods in health care faces technical and policy challenges. From a technical perspective, conducting value of information analyses, especially calculating the EVSI and the EVPPI in non-linear models, requires sophisticated

computations together with advanced expertise in economic evaluation and simulation techniques;(7) nevertheless, recent years have witnessed a progressive evolution and simplification of methods as well as advanced computing tools to reduce computational challenges.(8, 32-35) Another technical challenge is that certain assumptions are necessary when estimating value of information measures. These include the population expected to benefit from the technology, the lifetime of the technology, and the level of its implementation since the value of research is reduced if the results were not fully implemented.(4, 36-38) Several papers have addressed these assumptions and provided guidance to handle the uncertainty surrounding their estimates.(4, 36-38)

For the policy aspect, the main issue is that the decisions to adopt technologies and to conduct research are usually separate.(11) Claxton *et al.* noted this point in their first pilot study on value of information: “The key problem seems to be the policy environment where accountability and transparency for research prioritization and commissioning lags behind adoption and reimbursement decisions, and where there appears to be a separate remit for reimbursement and research decisions”.(11) Furthermore, the approach is relatively new and it will be some time before its value is realized by decision makers. Therefore, for the value of information analysis to be more incorporated into decision making frameworks, there is a need to create more awareness about the value of this approach and to align its methods with the needs of the decision making organizations.(7)

Conclusion

Value of information analysis is a systematic framework to measure decision uncertainty and assess whether there is sufficient evidence to support new technologies. Various value of information methods have been developed to inform decision making,

optimally designing research studies and setting research priorities. The application of VOI analysis in health care is increasing but remains limited due to conceptual, technical and policy challenges. Therefore, there is a need to create more awareness about this approach, simplify its current methods, and align them with the needs of the different jurisdictions in order for this approach to be incorporated into decision frameworks.

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Table 1: Illustrative example of the expected value of perfect information

Sampling scenario	Intervention A net benefit	Intervention B net benefit	Optimal choice	Opportunity loss	Maximum net benefit
1	\$ 1,000	\$ 1,400	B	\$ 0	\$ 1,400
2	\$ 1,200	\$ 1,100	A	\$ 100	\$ 1,200
3	\$ 900	\$ 1,300	B	\$ 0	\$ 1,300
4	\$ 800	\$ 1,200	B	\$ 0	\$ 1,200
5	\$ 1,100	\$ 1,000	A	\$ 100	\$ 1,100
Average	\$ 1,000	\$ 1,200		\$40	\$1,240

Figure 1: Optimal sample size determination using value of information methods

EVSI = expected value of sample information; ENBS = expected net benefit of sampling

Table 2: Prioritizing alternative research proposals using the value of information approach

Study	EVSI	Total cost	ENBS	ROI
Study 1	\$5,000,000	\$1,500,000	\$3,500,000	233%
Study 2	\$4,500,000	\$1,250,000	\$3,250,000	260%
Study 3	\$3,000,000	\$1,250,000	\$1,750,000	140%
Study 4	\$3,000,000	\$1,500,000	\$1,500,000	100%
Study 5	\$2,000,000	\$1,250,000	\$750,000	60%

EVSI =expected value of sample information; ENBS =expected net benefit of sampling; ROI = return on investment which is the ENBS divided by the total cost.