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Value of Information in Asia: Concepts, Current Use, and Future Directions



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ABSTRACT

Health technology assessment is a form of health policy research that provides policymakers with information relevant to decisions about policy alternatives. Findings from cost-effectiveness analysis (CEA) are one of the important aspects of health technology assessment. Nevertheless, the more advanced method of value of information (VOI), which is recommended by the International Society for Pharmacoeconomics and Outcomes Research and Society for Medical Decision Making Modeling Good Research Practices Task Force, has rarely been applied in CEA studies in Asia. The lack of VOI in Asian CEA studies may be due to limited understanding of VOI methods and what VOI can and cannot help policy decision makers accomplish. This concept article offers audiences a practical primer in

understanding the calculation, presentation, and policy implications of VOI. In addition, it provides a rapid survey of health technology assessment guidelines and literature related to VOI in Asia and discusses the future directions of VOI use in Asia and its potential barriers. This article will enable health economists, outcomes researchers, and policymakers in Asia to better understand the importance of VOI analysis and its implications, leading to the appropriate use of VOI in Asia.

Keywords: Asia, cost-effectiveness analysis, value of information.

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Introduction

Health technology assessment (HTA) is a form of policy research that examines short- and long-term consequences of the application of health care technology [1]. The primary goal of HTA is to provide policymakers with information relevant to decisions about policy alternatives. Throughout the industrial world in North America and Europe, HTA has been conducted at the national or multisystem level for several decades. It was, however, formally introduced in Asia during the late 1990s [2]. The early initiative of HTA in Asia was the formation of a special interest group on developing countries at the annual meeting of the International Society of Technology Assessment in Health Care in 1996. The special interest group, in turn, developed the Asian HTA network, which aims to pool available resources and maximize the resources of as many countries as possible. At present, several countries in Asia, such as Malaysia, Singapore,

China, South Korea, Taiwan, and Thailand, have formal HTA programs or organizations [2].

Findings from cost-effectiveness analysis (CEA) are one of the important aspects of HTA that inform policy decision making. Several CEA studies [3–9] have been conducted in Asia to inform policy decision making. Most of the CEA studies include standardized methods recommended by the International Society for Pharmacoeconomics and Outcomes Research and Medical Decision Making Modeling Good Practices Task Force [10], such as a base-case analysis and one-way and probabilistic sensitivity analyses. Although most studies were conducted using standardized methods, a challenge for implementing HTA in Asia is to help decision makers to set up an evidence-based appraisal system. It is an urgent need for improving the quality of HTA use in Asia.

In addition to the standardized methods such as base-case analysis and sensitivity analyses, the more advanced method of

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value of information (VOI) is recommended by the International Society for Pharmacoeconomics and Outcomes Research and Medical Decision Making Modeling Good Practices Task Force to prioritize further research. Nevertheless, VOI has rarely been applied in CEA studies in Asia. Briefly, VOI is a systematic decision-analytic approach aiming to inform optimal research design and prioritization. It is also used to inform decision makers in terms of assessing whether we should require additional information to inform decision making [11,12]. A systematic review [12] reveals that several studies reported VOI within CEAs for North American and European HTA. VOI is also recommended by the Patient-Centered Outcomes Research Institute to use as a decision-supportive tool for research topic prioritization [13]. VOI analysis can provide priority of research questions that have the greatest potential to improve population health [13]. There are, however, several methodological challenges in VOI application such as the high computational demands, complexities with nonlinear models, how to include structural uncertainty, and how to weave VOI into informing policy decision making. Even though VOI has been introduced and used in North America and Europe for many years, only a few published Asian CEA studies [14-16] disseminated VOI in an effort to inform policy decision making. The lack of VOI in Asian CEA studies may be due to limited understanding or uptake of CEA methods, which is a prerequisite of VOI. There are, however, several guidelines that provide important information on good research practices for conducting CEA [10,17-22]. Another possible reason of the lack of VOI in Asian CEA studies is understanding of VOI methods and what VOI can and cannot help policy decision makers accomplish. Given the efforts to solidify and standardize Asian HTA, we believe that now is a good opportunity for decision makers to gain a better understanding of VOI and to advocate for its application alongside conducting CEAs. Therefore, this article introduces the theory and concepts of VOI and provides a survey of HTA guidelines and literature related to VOI in Asia. Moreover, we propose future directions of VOI in Asia. This article will help in making VOI more accessible for readers and decision makers with limited experience or education of this topic. It illustrates a practical way to gain understanding of VOI and, in particular, expected value of perfect information (EVPI) through step-by-step calculations.

Theory and General Concepts of VOI

Health care systems face two policy questions on the adoption of a drug, technology, or intervention: 1) Should an intervention be adopted on the basis of existing evidence in the literature? 2) Is further evidence required to support this decision in the future? (Fig. 1) [23].

An analytic framework must meet the requirements to answer these two questions. The traditional rules of inference (e.g., P value < 0.05, confidence intervals, and credible intervals) fail to address both questions 1 and 2. Simply by rejecting a new technology on the basis of a P value or confidence interval, we are making a decision to treat with standard of care. The decision to treat a population of patients—and the selected treatment(s) among a group of mutually exclusive alternatives—cannot be deferred [24].

Given the objective of a health care system is to maximize health gain subject to a budget constraint, Claxton [24] has argued that a Bayesian decision-theoretic approach addresses both questions 1 and 2. The decision to adopt a technology after its regulatory approval should be based only on the posterior mean net benefit irrespective of whether differences lie outside a Bayesian credible interval (left side of Fig. 1, question 1). The distribution of mean net benefits is relevant only to decide

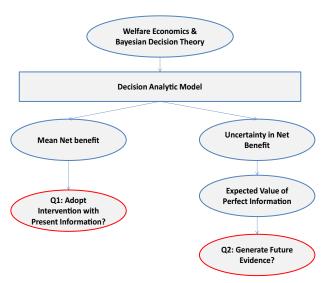


Fig. 1 – Evidence flow chart. Rooted in Bayesian decision theory, VOI can provide an analytic framework that is consistent with the policy-relevant questions faced by health care decision makers. VOI, value of information.

whether more information must be collected (right side of Fig. 1, question 2). As Claxton argued, this approach mirrors the sequential nature of decision making: making an initial decision, deciding to gather evidence, revising decisions after collection of new evidence, and again deciding whether more information is needed.

Application of the Bayesian decision-theoretic approach requires three tasks: 1) development of a decision-analytic model to represent the decision problem and to estimate mean net benefit, 2) a multivariate probabilistic analysis of this decision-analytic model to characterize the decision uncertainty, and 3) estimation of the value of additional information [23].

Once a decision-analytic model is developed, question 1 can be addressed by selecting the treatment alternative with the maximum net benefit as a function of expected cost, expected outcomes (e.g., quality-adjusted life-years [QALYs]), and a threshold (based on willingness-to-pay [WTP] or opportunity costs) (Fig. 2) where

Net monetary benefit=Health outcome \times Threshold-Costs. (1)

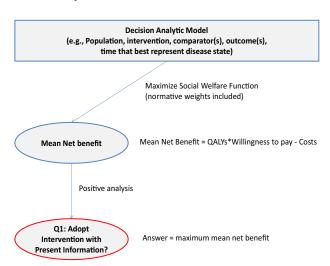


Fig. 2 - Addressing question 1. QALYs, quality-adjusted lifevears.

The maximum net benefit is based on a positive analysis or mathematical representation of which intervention option provides the most benefit given expected outcomes and a threshold (Fig. 2, question 1). In other words, decision-analytic modeling cannot determine the normative objectives, that is, how much to spend on health care, but it can provide guidance on achieving health care objectives given a set of proposed policies.

There will be uncertainty in net benefit (decision uncertainty) from model parameters propagated by the probabilistic sensitivity analysis (PSA) (Fig. 3). Therefore, adoption or rejection decisions must be made before the resolution of all uncertainty in the parameters of the model [25]. Given the true value of the model parameters is unknown, the EVPI for a particular patient is estimated by averaging the maximum net benefits for each iteration (perfect information) of a PSA when varying all uncertain parameters, less the maximum of the average net benefits for all iterations (present information) of the PSA (shown in Fig. 3, question 2). The population EVPI can be estimated using additional parameters in the model, such as the discount rate and the duration of treatment [25]. The population EVPI estimate provides decision makers and consumers of the research an upper bound on the value of generating additional research. In other words, the EVPI must be greater than the cost of acquiring additional evidence for a decision maker to fund more research.

Another concept called EVPI for parameters, or expected value of partial perfect information (EVPPI), provides an estimate of the value of acquiring additional information for a subset of parameters [25]. Similar to EVPI, EVPPI is estimated by averaging the maximum net benefits for each iteration of a PSA when varying a parameter or subset of parameters, less the maximum of the average net benefits for all iterations of the PSA. EVPPI can be used to identify specific parameters for which future research should focus on as end points in trials or prospective studies. Extensions to this framework include the expected value of sample information (EVSI) that provides the expected societal payoff to proposed research. For additional details on these advanced VOI analyses, please see studies by Claxton [24] and Claxton and Sculpher [25].

An Illustration of EVPI Calculation

This section demonstrates the steps involved in EVPI calculation through a hypothetical example. The example is streamlined to include only five Monte-Carlo iterations for illustrative purposes. Most EVPI calculations would include at least 1000 Monte-Carlo iterations. EVPI calculation requires three inputs: 1) WTP threshold, 2) health outcomes (usually QALY), and 3) cost. There are four steps of EVPI calculation: step 1, a computation of net benefit of each intervention for each Monte-Carlo iteration; step 2, a computation of maximum net benefit for each Monte-Carlo iteration; step 3, a computation of average expected net benefit for each intervention across all Monte-Carlo iterations; and step 4, a computation of EVPI. The net benefit of each iteration is calculated using Equation 1, whereas EVPI is calculated using the following equation (Equation 2):

where E is the expected value.

Figure 4 illustrates a step-by-step EVPI calculation using a hypothetical example of five Monte-Carlo iterations assuming that the WTP threshold is \$100,000 per QALY.

Step 1. A computation of net benefit of each intervention for each Monte-Carlo iteration: In this particular example, for intervention A (the first iteration), QALY is 1.00 and cost is \$75,000. Thus, the net benefit of this iteration is \$25,000. For intervention B (the first iteration), QALY is 1.25 and cost is \$125,000. Thus, the net benefit is \$0. The same computation is applied for all iterations.

Step 2. A computation of maximum net benefit for each Monte-Carlo iteration: Comparison of net benefit for each iteration across interventions is required for this step. For iteration 1 of this example, comparing the net benefit of interventions A and B, the maximum net benefit is \$25,000 (from intervention A). The same computation is applied for all iterations.

Step 3. A computation of average expected net benefit for each intervention across all Monte-Carlo iterations: In this step, average expected net benefits of interventions A and B and maximum net benefit are computed. In this example, average expected net benefits of intervention A, average expected net benefits of intervention B, and maximum net benefit are \$25,000, \$50,000, and \$60,000, respectively.

Step 4. A computation of per-person EVPI: As in Equation 2, EVPI is the difference in the average expected maximum net benefit of each iteration (\$60,000) and the maximum

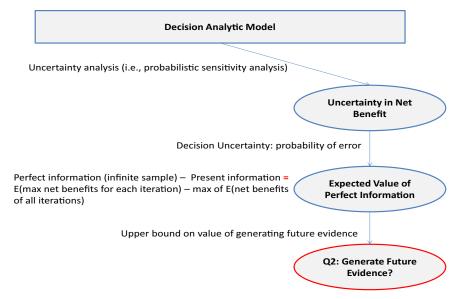


Fig. 3 - Addressing question 2.

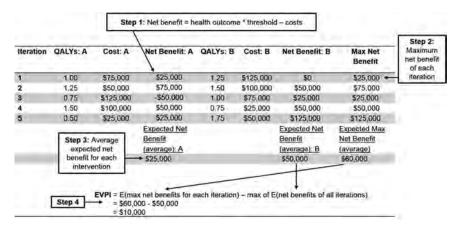


Fig. 4 – An illustration of the step-by-step EVPI calculation using a hypothetical example of five Monte-Carlo iterations. EVPI, expected value of perfect information; QALYs, quality-adjusted life-years.

of average expected net benefit across interventions (\$50,000). Thus, the per-person EVPI, or an estimate of the upper bound on the value of generating addition al research, for this example is \$10,000 (\$60,000 - \$50,000). In other words, additional research that costs less than \$10,000 per person should be considered to be conducted to reduce the decision uncertainty related to an adoption policy, whereas research that costs more than \$10,000 per person would not yield a positive return on investment.

A Survey of VOI Use in Asia

HTA Guidelines

We reviewed the HTA national guidelines from six countries in Asia, including China [2], Japan [19], Malaysia [26], South Korea [27], Taiwan [27], and Thailand [15]. We found that only the Thai HTA guideline incorporated VOI as a part of the guideline, whereas the other HTA guidelines in Asia did not mention or recommend VOI.

In the Thai HTA guideline [15], authors described the importance of EVPI, the calculation of EVPI with a hypothetical example, and a recommendation of EVPI use. In terms of EVPI recommendation, guideline authors suggested to use EVPI when policy decision makers have concern about uncertainty in the CEA and would like to know whether decision making should be delayed to collect additional information to reduce uncertainty.

Use of VOI in Cost-Effectiveness Studies

We surveyed the inclusion of VOI published in cost-effectiveness studies conducted in Asia by using the search engine PubMed from inception to August 2014. The key search terms were as follows: 1) value of information OR expected value of perfect information OR expected value of imperfect information OR expected value of sample information AND 2) Asia. Studies that met our search were further reviewed against the following criteria: 1) published in English, 2) was a cost-effectiveness study, and 3) included calculations of VOI in the publication.

A total of 10 articles were reviewed. Only three articles were included in this survey [14,16,28]. The rest were excluded because they were not cost-effectiveness studies. A summary of the characteristics of the included cost-effectiveness studies is presented in Table 1 and a summary of VOI use is presented in Table 2.

Among these three studies, two studies were conducted in Thailand [16,28] and the other study was conducted in South Korea [14]. Two of them were conducted using a Markov framework [14,28], whereas the other one was conducted using a hybrid model that consisted of a decision tree and a Markov model [16]. The technologies that were assessed in the studies varied. They included HIV vaccine, acupuncture, and hemodialysis and peritoneal dialysis.

All three studies determined the population EVPI, and the two studies from Thailand also determined EVPPI [16,28]. No study was conducted using EVSI to inform a policy decision. All studies used per capita gross domestic product to determine the WTP threshold; the threshold, however, varied by the indexed year.

Authors of the two Thai studies [16,28] suggested to use the VOI findings to prioritize future research for inputs used in the

Author	Country	Currency	Journal	Study design	Topic area	Technology
Leelahavarong et al. [16]	Thailand	Thai baht	BMC Public Health	Hybrid model (decision tree with Markov model)	Vaccine	HIV vaccine
Kim et al. [14]	South Korea	Korean won	BMC Complementary and Alternative Medicine	Markov model	Alternative medicine	Acupuncture
Teerawattananon et al. [28]	Thailand	Thai baht	Value in Health	Markov model	Medical device	Hemodialysis and peritonea dialysis

Table 2 – Use of	VOI in cost-	Table 2 – Use of VOI in cost-effectiveness studies.	dies.					
Author	Time horizon of VOI analysis	Number of cases per year used in VOI analysis	EVPI	EVPPI	EVSI	WTP threshold	Result of VOI	Policy implications
Leelahavarong et al. [16]	5 y	No report	Yes	Yes	No	100,000 THB per QALY	5,400 million THB at WTP threshold	Authors suggested to use the results from EVPPI to prioritize future clinical trials of the HIV vaccine but did not suggest to delay decision making
Kim et al. [14]	5 y	57,400	Yes	o Z	OZ	20 million KRW per QALY	180,000 million KRW at WTP threshold	Authors suggested to fund future research that evaluates the costeffectiveness of collaborative treatment of acupuncture and usual care but did not suggest to prioritize the future research or delay decision making
Teerawattananon et al. [28]	10 y	10,000	Yes	Yes	8 N	270,000 THB per QALY	0 THB at WTP threshold	Authors suggested that the result was certain at the WTP threshold. The authors, however, took the maximum EVPI as a proxy to prioritize future research for inputs
EVPI, expected value	e of perfect info	rmation; EVPPI, expec	ted value c	of partial pe	rfect infor	mation; EVSI, ex	rpected value of s	EVPI, expected value of perfect information; EVPPI, expected value of partial perfect information; EVSI, expected value of sample information; KRW, Korean won; QALY, quality-adjusted life-

year; THB, Thai baht; VOI, value of information; WTP, willingness to pay

cost-effectiveness model, whereas authors from the Korean study [14] suggested to use the VOI findings to fund future cost-effectiveness research. None of the authors suggested delaying a decision on the basis of VOI findings, even though selected findings suggested a high value for decision uncertainty that could be reduced by collecting additional information to update the model.

Even though VOI has been increasingly used worldwide as a supportive tool for policy decision making under uncertainty and to prioritize future research, it has been rarely used in Asian countries. On the basis of our rapid survey, only researchers from Thailand and South Korea have published VOI findings as an argument to prioritize future research.

Future Directions of VOI Use in Asia

As indicated by this review, VOI is not prioritized as one of the important components to include in general cost-effectiveness publications in Asia. Furthermore, only one of six HTA national guidelines incorporated VOI recommendations into its standardized methods.

HTA guidelines outside of Asia are mixed in terms of their recommendations for including VOI in cost-effectiveness publications. Given the complexities involved with conducting and reporting VOI findings, we believe that a targeted approach should be used. Following the case findings from Campbell et al. [29], when decision uncertainty is relatively low (in other words, when the HTA body will either adamantly accept the technology or adamantly reject the technology of interest because of a correspondingly attractive or unattractive incremental cost-effectiveness ratio), we advise against the efforts required to conduct and report VOI analyses. Nevertheless, when decision uncertainty is relatively high (in other words, when the HTA body has a difficult decision related to whether to adopt the technology and there is a relatively high degree of uncertainty in the incremental cost-effectiveness findings), and when the model input parameters are correlated resulting in a less linear model, VOI methods should be used and reported [29,30].

A benefit of reporting more VOI findings within a specific jurisdiction in Asia is that VOI findings yield further meaning and interpretation when compared across applications. A rank ordering of VOI may aid Asian HTA bodies in determining an efficient use of research resources to further reduce uncertainty in policy decisions. The methods used to produce EVPI and EVPPI are developed for software including Excel® (Microsoft) [23] and therefore should not place a huge burden on the analyst given that PSAs are already planned.

Barriers for conducting and reporting VOI within cost-effectiveness studies include the following: 1) a need to train cost-effectiveness analysts in this methodology (there are a limited number of analysts who understand and are able to conduct VOI analysis to inform research prioritization), 2) a need to educate decision makers of the importance of VOI methods and findings, 3) specification of a threshold (either WTP for a unit of health outcome or opportunity cost) to value a potential wrong adoption decision (methods exist for estimating an empirical threshold [31]), and 4) space limitations specified by peerreviewed journals of other dissemination mechanisms whereby VOI may not be determined to be important enough to disseminate. Because of the sophisticated methodology used in VOI analysis, it might be too complicated for policymakers and lead to the ignorance of the importance of VOI findings.

A critical appraisal of VOI is also important for policymakers to evaluate the validity of VOI. Because VOI is calculated from PSA of economic evaluations, the validity of VOI depends on the inputs used in PSA. VOI findings will be more accurate when inputs and their uncertainty are estimated accurately. Thus, we

recommend policymakers and analysts to assess how inputs are collected and how accurate inputs and their uncertainty are to evaluate the validity of VOI findings.

Conclusions

HTA is evolving with different stages across Asian countries. VOI analysis should be encouraged in situations such as when uncertainties around the findings exist because it will provide important information for future research direction. In particular, in regions where research resources are scarce, VOI should have even more importance and application. Nevertheless, VOI analysis globally remains in its infancy. There remains a need to understand the roles of VOI and its utilization for policy decision making globally and regionally, especially in Asia.

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