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Efficient Value of Information Calculation Using a Nonparametric Regression Approach: An Applied Perspective

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ABSTRACT

Background: Value-of-information (VOI) analysis provides an analytical framework to assess whether obtaining additional evidence is worthwhile to reduce decision uncertainty. The reporting of VOI measures, particularly the expected value of perfect parameter information (EVPPI) and the expected value of sample information (EVSI), is limited because of the computational burden associated with typical two-level Monte-Carlo–based solution. Recently, a nonparametric regression approach was proposed that allows the estimation of multiparameter EVPPI and EVSI directly from a probabilistic sensitivity analysis sample. **Objectives:** To demonstrate the value of the nonparametric regression approach in calculating VOI measures in real-world cases and to compare its performance with the standard approach of the Monte-Carlo simulation. **Methods:** We used the regression approach to calculate EVPPI and EVSI in two models, and compared the results with the estimates obtained via the standard Monte-Carlo simulation. **Results:** The VOI values from the two approaches were very close; computation using the regression method, however, was faster. **Conclusion:** The nonparametric regression approach provides an efficient and easy-to-implement alternative for EVPPI and EVSI calculation in economic models.

Keywords: Monte-Carlo simulation, nonparametric regression, value of information.

Introduction

Decision models are commonly used to evaluate the cost-effectiveness of health interventions. They are populated with input parameters estimated from various sources; nevertheless, the true values of these parameters are not known with certainty, which may result in suboptimal decisions [1]. The preferred approach to characterize decision uncertainty is to conduct probabilistic sensitivity analysis (PSA), whereby uncertainty is propagated in the model using Monte-Carlo simulation [2]. Decision uncertainty is then presented as the probability that each intervention has the highest expected net benefit (i.e., benefits minus costs). Nevertheless, an important additional step is to know whether a decision can be made on the basis of current evidence or whether additional research is required. This can be informed using value-of-information (VOI) analysis [3]. Measures of VOI include 1) the expected value of perfect information (EVPI), which is the maximum value of additional information to resolve all uncertainty in the parameters; 2) the expected value of perfect parameter information (EVPPI), which is the value of resolving uncertainty in a given parameter or set of parameters; and 3) the expected value of sample information (EVSI), which estimates the value of a particular data collection exercise (e.g., a randomized controlled trial with some chosen sample size) in reducing decision uncertainty [4].

EVPI calculation is straightforward given the PSA; nevertheless, although this measure is necessary, it is not sufficient to inform decisions because it represents only an upper bound of the value of additional research to resolve uncertainty [3]. Rather, it is important to know which parameters are contributing most to decision uncertainty, such that further research should focus on these. Here, the EVPPI for a parameter represents the value of eliminating uncertainty in that parameter, and therefore gives an upper bound on the value of a study to inform that parameter. The EVSI meanwhile represents the value of a given study design in reducing parameter uncertainty [5]. Comparing the EVSI with the expected cost of a research study establishes a sufficient condition to inform whether additional research is worthwhile. Unfortunately, the reporting of EVSI and EVPPI estimates in economic evaluations remains limited because of the perceived computational burden associated with these two measures [6–8].

The EVPPI for a single parameter or a group of parameters is typically calculated using a two-level nested Monte-Carlo simulation approach. This requires sampling values of the parameter(s) of interest in an outer loop, and then, conditional on each sampled parameter set, sampling from the joint conditional distribution of

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the remaining parameters in an inner loop. At each inner loop step the model is evaluated [9,10]. For EVSI calculation, plausible sets of data from the proposed future study of a given sample size are simulated in an outer loop, and then, conditional on each generated data set, the posterior distribution of the parameters is sampled in an inner loop. Again, the model is evaluated at each inner loop step [11,12]. The repeated sampling and evaluation of the model within the inner loop is time-consuming. Calculating EVSI values for a range of possible sample sizes could take days or even weeks depending on the complexity of the model [12–14]. Furthermore, it is often difficult to determine the number of simulations at each level to ensure adequate precision and to avoid the upward bias that results from the maximization over sampled quantities that occurs within the outer loop of the simulation [15]. Finally, the presence of parameter correlation or nonconjugacy between prior parameter distributions and proposed data likelihoods makes EVSI calculation even more difficult [11]. Here, Markov chain Monte-Carlo simulation (or any similar approach) would be necessary [6,7]. In some situations, most notably when using multilinear (i.e., sum-product type) models (e.g., decision tree) in which the net benefit is a linear function of the cost and effect parameters or in which the incremental net benefit is approximately normally distributed, one-level Monte-Carlo simulation or analytical equations can be used [11,16,17]. There is, however, a wide class of models for which these constraints do not apply.

Methods for efficient EVPPI calculation of single parameters have been developed. These show promise, but do not extend to groups of parameters simultaneously [18,19]. A method based on the numerical approximation of the posterior expected net benefit, conditional on sampled data, has been proposed as an efficient approach for EVSI calculation; it, however, requires significant skills and effort to write the necessary computer code [13,20]. Recently, Strong et al. [9,12] have proposed a more straightforward nonparametric regression approach for calculating multiparameter EVPPI and EVSI directly from a PSA sample. The method has the advantage in that the model does not need to be run as part of the EVPPI or the EVSI algorithm. Nevertheless, there is a need to demonstrate the value of this method in real-world cases and to compare its performance with the standard approach of the Monte-Carlo simulation.

In this study, we applied the nonparametric regression method to calculate the EVPPI and the EVSI in two decision models for two health care interventions. In addition, we compared the results and computation time with the estimates obtained using Monte-Carlo simulation.

Methods

The Two Economic Models

We conducted two cost-effectiveness analyses using two decision models constructed in TreeAge Pro (TreeAge Software, Inc., Version 2014 R1, Williamstown, MA). The full details of the two models and analyses can be found elsewhere [21,22].

Model 1: Negative pressure wound therapy in patients undergoing cesarean section

The first model was a decision tree for negative pressure wound therapy (NPWT) compared with hydrocolloid dressing in preventing surgical site infections after cesarean sections in high-risk (e.g., obese) women [22]. The modeled patients may develop surgical site infections that could be either superficial or deep. Patients could die or survive depending on the type of the infection developed (see Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.01.011). To populate the model, we systematically searched the literature and identified relevant evidence. Because of the scarcity of information on the effectiveness of NPWT in this setting, we combined the data on the relative effectiveness of the device from a pilot study (n = 92) on obese women undergoing cesarean sections with the data from a trial (n = 81) on NPWT in high-risk patients with various types of surgeries [22].

Model 2: Nutritional support for the prevention of pressure ulcers in hospitalized patients

The second model was a six-health-state Markov cohort model for nutritional support compared with standard hospital diet in preventing pressure ulcers [21]. Model duration was 1 year with a 1-day cycle length. Patients start the model with intact skin before they move sequentially between different stages of skin ulceration (i.e., closed wound to open wound). Furthermore, patients could die of any cause, be discharged, or remain hospitalized (see Appendix 1 in Supplemental Materials). We systematically searched and identified relevant evidence. We performed a meta-analysis of five trials (n = 1381) to estimate the relative effectiveness of nutritional support in preventing pressure ulcers compared with hospital diet [21].

The two models were probabilistic. Input parameters were assigned probability distributions: in general, beta distributions for probabilities and utilities, gamma distributions for costs and disutilities, and lognormal distributions for relative risks [21,22]. For the set of unknown input parameters (θ), each model predicted the net benefit (NB) for each intervention (i); thus, NB (i, θ) = willingness-to-pay × effect (i, θ) − *cost* (i, θ). The efficacy outcome in the two models was quality-adjusted life-years gained, and we set the willingness-to-pay threshold at $50,000 per quality-adjusted life-year. The preferred intervention would be the one with the maximum expected net benefit [$\max_i E_\theta$NB (i, θ)]. In each case, we performed a PSA using the Monte-Carlo simulation (10,000 iterations) to characterize decision uncertainty.

VOI Calculation

We calculated VOI measures using the standard Monte-Carlo simulation and the Strong et al. nonparametric regression approach for each of the two decision models. We also recorded, for each decision problem, the computation time for each VOI approach.

Methods to calculate VOI measures using Monte-Carlo simulations are described in detail elsewhere [11,23,24]. In short, we started our analysis by calculating the EVPI, which is the difference between the expected net benefit of a decision with perfect information and the decision based on current information [3]:

$$\text{EVPI} = E_\theta \max_i \text{NB}(i,\theta) - \max_i E_\theta \text{NB}(i,\theta) \quad (1)$$

The EVPPI for the parameter(s) of interest θ_I is the difference between the expected net benefit with perfect information on these parameters, conditional on the complementary set of other parameters θ_C, and the expected net benefit with current information [5,24]:

$$\text{EVPPI}_{\theta_I} = E_{\theta_I} \max_i E_{(\theta_C|\theta_I)} \text{NB}(i,\theta_I,\theta_C) - \max_i E_\theta \text{NB}(i,\theta) \quad (2)$$

For the pressure ulcer Markov model, we performed two nested Monte-Carlo simulation procedures with 1000 simulations in each loop. We found this number of simulations sufficient for the estimates to converge [24]. We assumed the NPWT model to be linear with no correlation between input parameters, and therefore a one-level simulation scheme was used in which we sampled from θ_I, but kept θ_C fixed at their prior mean [24].