Value of Information: We've Got Speed, What More Do We Need?

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Expected value of sample information (EVSI)[1] measures the average net-benefit gain from conducting new research and can be used to inform decisions on which new studies to fund and how best to design those studies. This helps avoid wasting resources researching treatments that were never likely to be cost-effective or conversely by adopting treatments that, if more evidence were collected, may be shown not to be cost-effective. However, the calculations in the general case rely on nested simulations, which can be very computationally demanding and even infeasible to compute in some cases. Since EVSI needs to be repeatedly computed over the potential study design space, this represents a clear barrier to the uptake of EVSI methods in practice.

In some special situations, algebraic solutions are available that avoid the inner simulation step.[2–4] More generally, meta-modeling, which attempts to build a model to approximate the relationship between the model inputs (on which a new study can provide information) and model outputs (net benefit), is a promising approach that can lead to substantial computational savings.[5,6] In this issue, 2 novel meta-modeling methods are proposed for the calculation of EVSI,[7,8] both of which require only a set of simulations created by standard probabilistic sensitivity analysis.

Strong and others[7] present a very elegant and computationally fast method that uses generalized additive models (GAM) and is general for any net benefit function. The method makes the reasonable assumption that there is a smooth relationship between the net benefit and sufficient statistics from a new research study. A more limiting assumption is that data collected in a new study can be summarized as a low dimensional set of sufficient statistics. This may not be the case in complex situations in which the data from new research studies may inform functions of model parameters, for example, when evidence is combined in a multiparameter evidence synthesis[9,10] such as a network meta-analysis.[11] When there are multiple, correlated parameters that new evidence informs, then there will be a tradeoff between accuracy through the inclusion of a sufficiently complex meta-model with interaction terms and computational speed. Perhaps in these situations, a combination of the algebraic approach[2–4] and the GAM approach[7] is a promising way forward, although this will require more work from the analyst in advance.

Jalal and Kuntz[8] present a computationally fast meta-modeling approach that explicitly allows for correlations between parameters. Their method assumes a normal distribution for incremental net benefit (INB), and they use a linear regression meta-model (a special case of the GAM model)[7] but found the linear approximation to be reasonable in the examples they explored, including a Markov model. Further work is needed to show whether approximate linearity holds for a broader range of models and evidence structures. INB is unlikely to be normally distributed, although if the time horizon for the economic evaluation is short, and INB has been collected alongside a randomized controlled trial (RCT) with a large enough sample size, then expected INB based on this sample can be assumed to be approximately normal. Another area for future research is to

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see how robust the methods are to nonnormality of INB and subsets of parameters that form INB.

It will be interesting to see how both of these methods compare across a range of examples: for different economic model structures, correlations between model parameter estimates, distributional assumptions on model parameters, and the relationship between data provided by new research studies and the model parameters. Note that such an exercise is challenging in those cases where there is no gold standard against which to compare the results because of computational infeasibility of the nested simulation approach.

It is not always necessary to compute EVSI. A first step should always to be to compute the expected value of partial perfect information (EVPPI), which provides an upper bound on EVSI, and only compute EVSI where EVPPI suggests there is likely to be value in further research. If EVSI does appear necessary, it may not need to be computed to a high degree of accuracy. The decision to fund a new RCT costing $3 million will not change whether the population EVSI is estimated to be $1.2 million or $1.5 million. Even in cases in which we have identified that it is worth funding a new study and we want to find the optimal study design, the net returns from a study of a given design tend to be very flat near the optimum.[12] As long as any bias in EVSI computation does not vary systematically with study design, a pragmatic approach that chooses a study design that is conservative (e.g., lowest sample size) within a given tolerance around the optimum may be fairly robust to the computational method used for EVSI.

A more fundamental concern is that EVSI, and reimbursement decisions in general, are sensitive to uncertainty in the model structure.[13–16] Methods have recently been proposed to compute the expected value of reducing structural, as well as parameter, uncertainty.[17,18] However, these methods do not address the concern that EVSI itself, and thus the assessments of the value of reducing uncertainty, change with structural assumptions. Much valuable research could be conducted investigating how EVSI varies with structural assumptions and the impact on decision making.

A major attraction of the meta-modeling approach is that it is general and can be used like a ''black box.'' Thus, it could be included in standard software, for example, the bCEA package for cost-effectiveness analysis in R[19] and online applications (e.g., http://savi.shef.ac.uk/SAVI/).

If EVSI is to be used in practice to inform funding decisions, research funding committees need to embrace the concept—this may well prove to be a bigger barrier than computation. Although reimbursement committees are familiar with critically appraising economic models, research funding committees are less so, and the black box feature, desirable for computational efficiency, may lack the transparency required by committee members.[20] EVSI assesses the merits of new research in terms of cost-effectiveness. However, statistical significance is still important to convince clinicians of treatment efficacy, and we would recommend that value-of-information analyses be conducted alongside standard power calculations, so that both clinical and cost-effectiveness can be considered. More applied examples are needed to increase familiarity of committees with EVSI methods, together with training for committee members so that they can critically appraise the analyses and use them to inform their decision making.

The credibility of an EVSI analysis relies on the credibility of the economic model and its inputs. Developing a model with input from key stakeholders, identifying model inputs, and performing the computations requires resources, and it is not clear how the additional work required by EVSI should be funded. One possibility is to require value-of-information analyses to be conducted alongside health technology appraisals, and in fact they often are. However, there needs to be a mechanism for the research recommendations from these reports to feed into funding calls for research proposals or to be considered when assessing researcher-initiated proposals. Another possibility is for value-of-information analyses to be conducted during a feasibility phase of an RCT, which seems a natural place for such work, although existing evidence may be scarce and evidence collected in a feasibility trial may lack generalizability, making it difficult to quantify uncertainty.[3] Although trialists may be unenthusiastic if the analyses suggest there is no value in a full trial, this allows them to focus on more fruitful questions for primary research. Another option is for value-of-information analyses to be directly commissioned to answer specific questions, for example, to help inform decisions that involve a large investment[21] or areas in which there is conflicting existing evidence.[22] Finally, reimbursement agencies could require value-of-information analyses to be presented in manufacturer submissions of cost-effectiveness. This has been suggested in the context of making ''only in research'' decisions to be made where a new product can only be used in the collection of new evidence.[23]

This is a very exciting time for value-of-information methods, and now that the computational issues are being resolved, it's time for the research funding community to consider using the methods routinely in their decision making. Given the scarcity of research resources, it is important that they are allocated as efficiently as possible to generate the research needed to deliver health care that provides the best value for money to patients.

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