Addressing Decision Uncertainty in a Cost-Effectiveness Model of Opioid Use Disorder Treatments: Estimating the Value of Information and the Sample Size to Provide It

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Introduction/Objectives

A trial-based cost-minimization analysis (CMA) of office- or clinic-based methadone (MO and MC respectively) and office-based buprenorphine (BO) to treat opioid use disorder (OUD)[1] showed MC as optimal. Our de novo cost-effectiveness analysis (CEA) used the underlying CMA data as inputs and incorporated effectiveness measures that were not statistically different.[2] Under the CEA, optimal treatment changed to MO and decision uncertainty (based on a probabilistic sensitivity analysis (PSA)) was substantial compared to the decision uncertainty assessed for the CMA. Willingness-to-pay (WTP) for an additional patient retained on treatment ($7000) was identified in the literature.[3]

In a value of information analysis, we examine sources of uncertainty by quantifying expected value of partial perfect information (EVPPI) for model parameters of interest (POI). We estimate the expected value of sample information (EVSI) to inform appropriate sample size to reduce uncertainty in the EVPPI-identified POI.

Methods

We developed an Excel® model and explored EVPPI for effectiveness and cost parameters in 6 groups. Groups subject to EVPPI estimation included the 3 retention on treatment efficacies as one group and 5 individual resource use inputs.

The EVPPI estimation applied a two-level Monte Carlo sampling procedure, where within an outer loop a value is drawn for one of the outer-loop parameters or sets of parameters if in a group (i.e., parameters subject to EVPPI estimation), and an inner-loop of 1,000 PSA iterations is performed for each outer-loop draw. Net monetary benefit (NMB) was recorded for each iteration. The process was repeated for 100 draws of each outer-loop parameter, resulting in the necessary information to calculate EVPPI per input.

The EVPPI results informed which parameter(s) were the greatest contributors to decision uncertainty, and therefore the best candidates to be subject of further research to refine their estimates and reduce uncertainty. We then explored the patient-level expected value of sample information (EVSI) for the POI with significant EVPPI in order to identify the appropriate sample size for a future study.

Rather than simply choosing the sample size that maximizes EVSI, one must balance those gains against the cost of conducting the proposed research. The EVSI was scaled to a population level (denoted P_EVSI) by accounting for the total patient population that may benefit from research that reduces uncertainty. A maximum expected net gain from sampling (ENGS) was estimated by setting marginal cost of an additional study participant equal to the expected marginal benefit from a study of that size. We simulated various sample sizes (n), calculating for each the P_EVSI, the per patient trial cost and the resulting ENGS, where:

$ENGS_n = P\_EVSI_n - \text{Trial Cost}_n$.

Due to significant variability in the simulation and limitations to computing time, we approximated ENGS and P_EVSI by fitting polynomial equations to the simulated values.

Results

The results for the EVPPI estimates are displayed in Figure 1, and the results for EVSI are shown in Figure 2.

Figure 1 displays the EVPPI estimated for each of the six POI considered in the analysis. Each has a separate EVPPI estimated depending on WTP. WTPs of $3,000; $7,000; and $10,000 were considered. The parameters relating to treatment effectiveness as measured by retention on treatment had substantial associated EVPPI, whereas the EVPPI of the other variables was comparatively negligible.

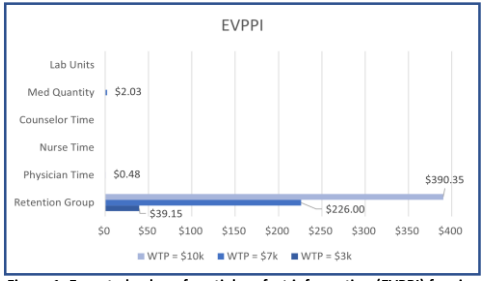

Figure 1: Expected value of partial perfect information (EVPPI) for six parameters of interest at three willingness to pay (WTP) thresholds

Figure 2 presents the P_EVSI and ENGS. Due to lengthy computing times in EVSI estimation, we do not estimate EVSI for every individual sample size (i.e., increasing by increments of 1) but rather estimate a collection of sample sizes across a range and allow the EVSI and ENGS estimates represented as points on our graphs to guide us in fitting curves for the EVSI and ENGS functions, displayed in the blue and gray dotted lines, respectively.

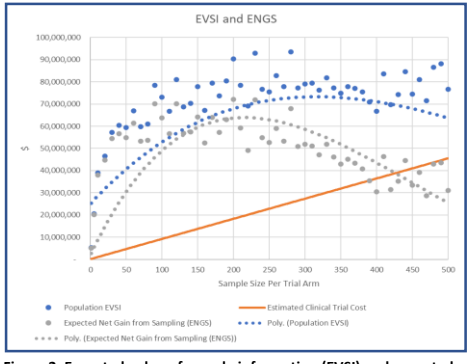

Figure 2: Expected value of sample information (EVSI) and expected net gain from sampling (ENGS) for a new study on retention; assumes a willingness to pay (WTP) threshold of $7,000

In calculations of NMB within the ENGS and EVSI estimation procedure, we adopted a WTP of $7,000 per additional patient retained. To identify the recommended sample size for a new study that gathers data on retention, we find the approximate sample size for which the ENGS curve is maximized. Based on this value of information analysis, the study sample size per treatment arm that would efficiently reduce the uncertainty generated from the effectiveness inputs is estimated at an n of 225.

Conclusions

The EVPPI analysis for the decision problem of comparing MO, MC, and BO to treat OUD in a CEA framework identifies the effectiveness inputs as those contributing most to uncertainty. The EVSI analysis indicates the efficient sample size for a study to reduce this uncertainty is approximately n = 225. For the CMA, with EVPPI of zero, EVSI and ENGS would also be zero, further supporting the value of the CEA.

The literature provides examples for estimating EVPPI, EVSI, and ENGS, making them fairly straightforward to implement.[4] A potential barrier is computing time (substantial using Excel®). Our estimates were not precise given a restricted set of simulations that necessitated curve-fitting. Implementation of these VOI methods more generally can provide insights to clarify the potential for resolution of uncertainties in health economic models.

References

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