‘Expected Value of Perfect Information’ calculations in health economics

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Introduction The field of economic evaluations in health economics is undergoing a dramatic change at the moment. New methods have been developed, other methods have been refined. Decision analytic models have become a commonly applied tool to answer research questions that cannot be addressed by clinical trials because of too short follow-up times or because adequate data is not available [1]. Sensitivity analysis has always played an important role in decision analytic modelling. One-way sensitivity analysis is still the method of choice for the analysis of methodological uncertainty (e.g. the analysis of different starting parameters in the model). A method for the analysis of parameter uncertainty (second order uncertainty) is probabilistic sensitivity analysis (PSA) [2;3]. Probability distributions are fitted to model parameters from input data. For PSA the decision model is then recalculated many times (e.g. 1000 iterations are performed). From all model runs the overall result will be calculated and can be expressed as the incremental cost-effectiveness ratio or the incremental net benefit statistic.
It is now the accepted standard to calculate the proportion of iterations in which the model yields a favourable cost-effectiveness estimate for a range of different willingness to pay values (threshold values) and to summarise the result in a cost-effectiveness acceptability curve (CEAC) [4]. The CEAC can also be interpreted as showing for a given threshold value the probability that the intervention is cost-effective. Although possible in theory, a probability that the intervention is 100% cost-effective will never be observed in reality. This implies that there is always a possibility of considering an intervention cost-effective when in fact it is not. This is due to the uncertainty that was explicitly taken into account using probability distributions instead of point estimates for the model input parameters. With perfect information (no parameter uncertainty) there would not be the possibility of making the “wrong” decision. Expected value of perfect information (EVPI) calculations allow us to quantify in a monetary way the possible loss that arises by making the wrong decision, and therefore represent the maximum amount of money that is reasonable to be spent on further research to completely eliminate uncertainty for this decision problem [5]. EVPI calculations will be shown for a probabilistic decision analytic model that was constructed to assess the cost-effectiveness of risedronate, a drug from the class of bisphosphonates that is used for the prevention and therapy of osteoporosis.
Methods A probabilistic Markov model with 7 health states was developed. All transition probabilities, costs, utilities and other model parameters were taken from published studies or official sources. In cycle zero a cohort of 10000 patients was modelled to live in a health state that represents female patients aged 70 at risk of a hip, wrist or vertebral fracture living independently at home. These patients were also modelled facing a monthly risk of a natural death. Hip fracture patients additionally face the risk of dying due to their fracture or may become dependent (i.e. require home care) or may need to move to a nursing home. The relative risk of having a fracture when under risedronate and calcium and vitamin D (compared to calcium and vitamin D alone) was taken from a meta-analysis. In the decision model lognormal distributions were fitted to the relative risk parameters. Parameter uncertainty in the transition probabilities was represented by beta distributions that were applied to the data by the method of moments fitting. Second order uncertainty with regards to the cost data was modelled by gamma distributions. Parameter uncertainty in quality of life estimates was represented by beta distributions. PSA was performed with 5000 Monte Carlo simulations.
Results The incremental cost-effectiveness ratio for risedronate treatment when compared to no treatment is CHF 110’982 per QALY. At a willingness to pay level of CHF 80’000 per QALY risedronate has a probability of 33% of being cost-effective. At the same threshold level treating 10’000 patients with risedronate provides an incremental net monetary benefit of CHF -7’614’108 (95% confidence interval CHF -40’660’215 to CHF 30’282’167). The results show that the uncertainty surrounding the cost-effectiveness estimate is large. Although the baseline decision should in this case be to not provide risedronate, the upper boundary of the confidence interval would suggest that there is a potential net monetary benefit of risedronate therapy of CHF 30m per 10000 treated patients. Even at a threshold value of CHF 150’000/QALY where providing risedronate is seen as the optimal strategy, there is a 42% probability that risedronate is regarded as cost-effective when in fact it is not. Using an one-level approach the total EVPI for this decision is CHF 9.5m per 10000 treated patients at a threshold level of 80’000/QALY. The expected value of sample information (EVSI) shows that the relative risk parameters contribute the most towards total parameter uncertainty with an EVSI of more than CHF 7m per 10000 treated patients. Quality of life estimates also have a substantial impact on total parameter uncertainty, the other subgroups such as costs and transition probabilities only have a relatively low impact on total EVPI.
Discussion Using a decision model that incorporates PSA the uncertainty in the decision problem, whether risedronate is cost-effective or not, could be quantified by stating the probability that the intervention will be cost-effective for a given willingness to pay level. The calculation of EVPI allowed to quantify the cost of uncertainty surrounding the decision in a monetary way. The further breakdown into subgroups when calculating the EVSI allows us to identify which groups of parameters have the highest impact on total parameter uncertainty. This is helpful for prioritising future research. As it is difficult to assess whether the current level of evidence is large enough to support the implementation of a new strategy (e.g. reimbursement of a new pharmaceutical drug) this framework shows the potential value of further research (by research area) for the decision under analysis [6].

Literature

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