Cost-Effectiveness Analysis in Veterinary Medicine: Illustration With Packed Cell Value in the Prognosis of Horse Surgical Colic in Belgium

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ABSTRACT
Techniques of cost-effectiveness analyses were applied to determine whether or not it is economically efficient to measure the packed cell volume (PCV) on a colic horse before deciding on abdominal surgery. The effects of this decision of uncertainty on the estimated values of the parameters (probability of survival after surgery, surgery costs, PCV positive predictive value, and length of survival after surgery) were considered along with the monetary values of collecting additional information on those parameters. The effects of uncertainty on the incremental net benefits of each alternative were depicted by tornado diagrams, cost-effectiveness acceptability curves, and posterior probability distributions. The worth of additional information was computed as the expected values of perfect and sampling information. Given previously published results, the best PCV cut-off point to distinguish between survivors and non-survivors was at 44%. At this threshold, the most economically effective alternative is to measure PCV before surgery providing the owner is willing to pay less than €672 for each year the horse survives. Uncertainty on probability of survival after surgery largely influenced the decision whether or not to measure the PCV, but one should spend at most €381 in research to reduce this uncertainty. A study of postoperative survival of 500 colic horses would ensure an expected gain of €370 associated with a reduction in uncertainty.

INTRODUCTION
Cost-effectiveness analysis is a tool that enables a decision maker to make informed choices. For the veterinarian, this may consist of choosing to treat or not to treat a sick animal, to perform or not to perform a clini-
cal test before a surgical act, or to decide whether or not to investigate further the basis of an unknown disease. In cost-effectiveness analysis, the costs and benefits of the different alternatives are measured and compared, their relative efficiency is assessed, and the most cost-effective alternative is preferred (assuming the decision maker is rational). Costs are measured in monetary units and benefits are measured in terms of clinical outcome (eg, mortality, morbidity, time for reoccurrence of the disease) to which a monetary value is assigned, value that reflects the decision maker’s maximum willingness-to-pay for that clinical outcome. At the end of the analysis, economic results can be summarized in terms of incremental net benefit (INB), that is, the difference in increments in effectiveness and in costs.

For a number of reasons, costs and effects are seldom known with certainty. Uncertainty on the model arises from 2 sources: model development and the values of the parameters. In this article, we concentrated on parameter uncertainty and accepted the model as given. Parameter uncertainty is of first degree when uncertainty is about the true values of the parameters (eg, unobservable values of costs and effects or disagreement among experts). Parameter uncertainty is of second degree when it is associated with sampling variation (eg, limited samples available to estimate the true values of costs and effects). Deterministic analyses, in which costs and effects are varied over their possible range, are often used to take account for the first degree uncertainty while stochastic simulation methods, in which a distribution is specified for each cost and effect, consider the second degree uncertainty.

To reduce uncertainty, the decision maker may gather additional information; however, this means incurring additional time and monetary costs. The question then arises whether gathering this additional information is valuable economically. The expected value of perfect information (EVPI) represents the value of completely eliminating the uncertainty (ie, collecting information with perfect accuracy). It is the upper limit to the amount the decision maker would be willing to pay for any additional information. But obtaining perfect information is nearly impossible. More often, the decision maker will collect more data and compute the expected value of sample information (EVSI) (ie, the additional expected profit possible through knowledge of the sample information).

The goal of the present study was to illustrate cost-effectiveness analyses with an example on the prognostic value of packed cell volume (PCV) in equine surgical colic. The selected alternatives were whether or not to carry out the PCV test before deciding to undertake the surgery, given that the decision to perform surgery involves a trade-off between the immediate expenses posed by the veterinary act and the risk of death. The goal was not to give veterinarians strict indication on the prognosis value of colic surgery based only on PCV pre-surgery values but to illustrate the potentials of cost-effectiveness analyses in urgency veterinary medicine.

**MATERIALS AND METHODS**

An analysis of costs and effects of surgery for colic of the large intestine in horses was conducted. In this study, the number of years by which life is extended ($Y_e$) after surgery was used as the measure of effectiveness; costs were associated with surgery ($C_s$) (ie, cost of surgery and loss of work value) and with the PCV clinical test ($C_p$). The same value for $Y_e$ was assumed for horses surviving colic surgery and for non-colic horses. The strategy “no test” consisted of surgical treatment of colic without PCV screening. It was compared with the strategy “test,” consisting of surgery after a positive PCV screening and no surgery if the PCV result was negative (Figure 1).

In the strategy “no test,” survival after surgery was achieved at a probability of $p_{eff}$. In the strategy “test,” surgery was
executed when the test was positive at a probability of $p_{tp}$ and survival was attained at a probability of $p_{tp\_eff}$ (the test’s positive predictive value). Assuming that horses will die without surgery, the effectiveness ($E_\alpha$) and cost ($C_\alpha$) associated with the strategy “no test” were:

$$E_\alpha = p_{\text{eff}} \times Y_\alpha$$

and

$$C_\alpha = C_S,$$ respectively.

For the strategy “test,” effectiveness ($E_T$) and cost ($C_T$) were:

$$E_T = p_{tp} \times p_{tp\_eff} \times Y_\alpha$$

and

$$C_T = (p_{tp} \times C_S) + C_p,$$ respectively.

**Baseline Analysis**

For each proportion parameter ($p_{tp}$, $p_{\text{eff}}$, and $p_{tp\_eff}$), a base-value (ie, the reference case) was identified from results of a study of PCV in horses referred at the veterinary hospital of the University of Liège (Belgium) for surgical colic of the large intestine. Base-values were obtained for $C_S$ and $Y_\alpha$ after a search on Google and Medline on November 22, 2004 (Table 1). Then, values for the incremental net benefit (INB) were computed as:

$$\text{INB}_K = K \times (E_T - E_\alpha) - (C_T - C_\alpha),$$

for different values of $K$, where $K$ is the monetary value for 1 horse-year survived. The most cost-effective alternative was the strategy that led to the highest $\text{INB}_K$.

**Analysis of Uncertainty**

To analyze the effects of uncertainty on the parameters on the selection of the most cost-effective alternative (“test” or “no test”), 2 analyses were conducted. In the first analysis (first degree of uncertainty), parameter values were varied independently over their possible ranges to obtain highest and lowest $\text{INB}_K$. Maximum and minimum probabilities of survival after surgery were set at 100% and 50%, respectively. The cost of surgery varied from €1,500 to €7,500, and the length of survival after surgery ranged from 2 to 40 years (Table 1). The cost of PCV screening remained fixed at its current value of €10. Tornado diagrams depicted the effects of this type of uncertainty on $\text{INB}_K$.

In the second analysis (second degree of uncertainty), all parameter values were randomly sampled from different prior distributions and the incremental costs and effects were recalculated over 300,000 simulations. For $p_{\text{eff}}$, $p_{tp}$, and $p_{tp\_eff}$, prior distributions were Beta ($\alpha$, $\beta$) with $\alpha = r_0 + 1$ and $\beta = n_0 - r_0 + 1$, with $r_0$ = base-value for number of successes and $n_0$ = base-value for number of trials. The variables $\ln(C_S)$ and $\ln(Y_\alpha)$ were each assumed to be a random sample from a Normal ($\mu$, $1/\tau$) population with prior specifications $\mu \sim \text{Normal} (\mu_0, 1/n_0\tau)$ and $\tau \sim \Gamma (\eta, \delta)$, with $\eta = 4$ and $\delta = \eta\delta^2$, $\mu_0 = \ln(\text{base-value}) - 1/2\delta\tau_0$, and $\tau_0 = \log (1 + [\text{range}/(2 \times 1.98)])^2$, assuming 90% of the values for $\ln(C_S)$ and $\ln(Y_\alpha)$ are within 2 standard deviations from their expected values. Base-values and ranges were from Table 1 and the value for the degrees of belief $\eta$ was obtained by trial and error. The prior distributions were chosen to compute explicitly the conjugated posterior distributions for $\text{INB}_K$. Uncertainty intervals were estimated from the simulated data.

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*Figure 1. Decision tree displaying the alternatives of the horse colic problem.*
by taking the end points of a 95% interval around the average value for INB_k over all iterations. Cost-effectiveness acceptability curves (CEAC) were also constructed in which the probability, based on the available evidence, that INB_k is positive is plotted against K. These probabilities were computed, for each value of K, as the proportion of iterations in which the strategy “test” had positive INB_k.

**Value-of-Information Analysis**

Finally, the worth of obtaining additional information on the unknown parameters (CS, YE, p_eff, p_tp, and p_tp_eff) was computed as the EVPIK and EVSIK. The algorithm proposed by Ades et al\(^\text{17}\) was chosen to get EVPIK and EVSIK.\(^\text{18}\) It consists of drawing a sample from the prior distribution of the parameter on which more data are to be collected and a sample from the predictive distribution of the sufficient statistics arising from a new dataset of size n, given the current value of the parameter. The prior distributions were those obtained in the analysis of the second degree of uncertainty. The predictive distributions for CS and YE were log-normal Logn(\(\mu_0\), \(1/\sigma_\tau\)). The predictive distributions for r_eff, r_tp, and r_tp_eff were binomial: Bin(p_eff, n), Bin(p_tp, n) and Bin(p_tp_eff, n_tp), respectively. Then,

\[
\text{EVPI}_k = \tilde{E}(\text{max INB}_k) - \text{max } \tilde{E}(\text{INB}_k),
\]

and

\[
\text{EVSI}_k = \tilde{E}_D(\text{max INB}_k) - \text{max } \tilde{E}(\text{INB}_k),
\]

where \(\tilde{E}(\text{max INB}_k)\) is the expected value under perfect information, \(\text{max } \tilde{E}(\text{INB}_k)\) is the expected value under current information, and \(\tilde{E}_D\) is the expected value under imperfect information obtained from data D.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Base-Value</th>
<th>Range</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery costs (€)</td>
<td>(C_s)</td>
<td>4,000</td>
<td>1,500 to 7,500</td>
<td>logN (4,000, 1,515)</td>
</tr>
<tr>
<td>Test cost (€)</td>
<td>(C_p)</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of life extended after surgery</td>
<td>(Y_E)</td>
<td>19</td>
<td>2 to 40</td>
<td>logN (19, 5)</td>
</tr>
<tr>
<td>Proportion of horse surviving surgery (%)</td>
<td>(p_{\text{eff}})</td>
<td>62</td>
<td>50 to 100</td>
<td>Beta (61, 99)</td>
</tr>
<tr>
<td>Proportion of horse with packed cell volume less than (%)</td>
<td>(p_{\text{tp}})</td>
<td>2</td>
<td></td>
<td>Beta (2, 99)</td>
</tr>
<tr>
<td>Proportion of surviving horse among those with packed cell volume less than</td>
<td>(p_{\text{tp_eff}})</td>
<td>1.00</td>
<td></td>
<td>Beta (2, 11)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Base-Value</th>
<th>Range</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>27%</td>
<td></td>
<td>0.79</td>
<td></td>
<td>Beta (11, 14)</td>
</tr>
<tr>
<td>32%</td>
<td></td>
<td>0.74</td>
<td></td>
<td>Beta (26, 35)</td>
</tr>
<tr>
<td>44%</td>
<td></td>
<td>0.74</td>
<td></td>
<td>Beta (52, 70)</td>
</tr>
<tr>
<td>49%</td>
<td></td>
<td>0.72</td>
<td></td>
<td>Beta (58, 82)</td>
</tr>
<tr>
<td>52%</td>
<td></td>
<td>0.69</td>
<td></td>
<td>Beta (60, 87)</td>
</tr>
<tr>
<td>55%</td>
<td></td>
<td>0.65</td>
<td></td>
<td>Beta (61, 94)</td>
</tr>
<tr>
<td>61%</td>
<td></td>
<td>0.62</td>
<td></td>
<td>Beta (61, 99)</td>
</tr>
</tbody>
</table>
RESULTS

In the study of Gruulke et al., a horse was classified either as a survivor if it was discharged from the clinics, or as a non-survivor. Average blood PCV was 30.29% (standard deviation [SD] = 6.18) among survivors and 45.03% (SD = 8.77) among non-survivors. Consequently, the PCV test was considered positive when PCV was below some threshold values. A receiver operating curve (ROC) displaying the sensitivity and specificity of the test is shown in Figure 2. The best PCV cut-off point to distinguish between survivors and non-survivors was at PCV = 44%, as determined by the highest Youden index, with 73% of the cases correctly classified and a kappa value of 33%. Therefore, unless stated otherwise, this PCV value was chosen in the analysis.

Baseline Analysis

Whatever the willingness-to-pay (K) for 1 survived year (Y_s) and the PCV limit, the strategy “test” was less costly and less beneficial than the strategy “no test.” It was highest at K= €1 with INB1 = €1,160. This value corresponded to the difference in net benefits between both alternatives, with –€2,819 for the “test” and –€3,979 for the “no test” alternative. The INBk decreased linearly as K increased and became negative for K > €672.

Analysis of the First Degree of Uncertainty

Uncertainty on surgery costs had highest effects on INB1 for all PCV values (Figure 3). The INB1 declined to €428 for C_S = €1,500 and increased to €2,185 when C_S = €7,500. The effect of uncertainty on surgery costs remained constant at all K values, but the effect of uncertainty on YE, p_tp_eff, and p_eff increased as K increased. For
example, INB$_{250}$ = €1,116 for $Y_E = 2$ years and INB$_{250}$ = €593 for $Y_E = 25$ years; INB$_{250}$ = €1,044 for $p_{eff} = 55\%$ and INB$_{300}$ = –€1,093 for $p_{eff} = 100\%$.

### Analysis of the Second Degree of Uncertainty
Prior distributions for $p_{eff}$, $p_{tp}$, $p_{tp_{eff}}$, $C_s$, and $Y_E$ are shown in Figure 4 with the corresponding posterior distributions for INB$_K$ when $K = €100$, €1,000, and €1,500. Prior averages and 95% confidence intervals (in parentheses) for the proportions were $61.40\%$ (61.38–61.42) for $p_{eff}$, $70.30\%$ (70.29–70.32) for $p_{tp}$, $73.60\%$ (73.58–73.62) for $p_{tp_{eff}}$, €3,751 for $C_s$, and $18.07$ (18.06–18.07) years for $Y_E$. The posterior means for INB$_K$ and their standard errors for PCV = $27\%$, $38\%$, and $52\%$, and for $K = €1$, €100, €500, €1,000, and €1,500 are in Table 2. Note that standard errors were lower at low than at high K values. In Figure 5, the CEAC showed that the probability of a positive INB$_K$ was $100\%$ for $K \leq €100$ at any PCV values. The probability then decreased. It was close to zero at $K = €500$ for PCV = $27\%$, and reached $30\%$ at $K = €1,000$ for PCV = $44\%$ and $55\%$ at $K = €1,000$ for PCV = $52\%$.

### Value-of-Information Analysis
The values for EVPI$_K$ were higher than €1,000 for $K \leq €100$, but they became almost zero at $K = €500$ for PCV = $27\%$ and at $K = €800$ for PCV = $38\%$ (Figure 6). From Table 2, it can be seen that INB$_K$ and EVPI$_K$ were identical as long as $pr(INB_K > 0) = 100\%$ and that EVPI$_K$ became greater than INB$_K$ for value of
Table 2. Posterior Means (Standard Errors) for Incremental Net Benefit (INB) of the Strategy “Test” Over the Strategy “No Test,” the Expected Value of Perfect Information (EVPI), and the Probability of a Positive INB for Different Monetary Values of 1 Survived Year (K).

<table>
<thead>
<tr>
<th>K = €1</th>
<th>PCV = 27%</th>
<th>PCV = 38%</th>
<th>PCV = 44%</th>
<th>PCV = 52%</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVPI (€)</td>
<td>3667 (0.76)</td>
<td>2189 (0.45)</td>
<td>1091 (0.23)</td>
<td>446 (0.09)</td>
</tr>
<tr>
<td>INB (€)</td>
<td>3667 (0.76)</td>
<td>2189 (0.45)</td>
<td>1091 (0.23)</td>
<td>446 (0.09)</td>
</tr>
<tr>
<td>pr(INB &gt; 0) (%)</td>
<td>100 (0.00)</td>
<td>100 (0.00)</td>
<td>100 (0.00)</td>
<td>100 (0.00)</td>
</tr>
<tr>
<td>K = €100</td>
<td>EVPI (€)</td>
<td>2606 (0.80)</td>
<td>1644 (0.51)</td>
<td>918 (0.32)</td>
</tr>
<tr>
<td>INB (€)</td>
<td>2606 (0.80)</td>
<td>1644 (0.51)</td>
<td>918 (0.32)</td>
<td>416 (0.24)</td>
</tr>
<tr>
<td>pr(INB &gt; 0) (%)</td>
<td>100 (0.00)</td>
<td>100 (0.00)</td>
<td>100 (0.00)</td>
<td>100 (0.00)</td>
</tr>
<tr>
<td>K = €500</td>
<td>EVPI (€)</td>
<td>5.17 (0.11)</td>
<td>81 (0.40)</td>
<td>381 (0.81)</td>
</tr>
<tr>
<td>INB (€)</td>
<td>-1679 (1.43)</td>
<td>-561 (1.27)</td>
<td>219 (1.18)</td>
<td>293 (1.14)</td>
</tr>
<tr>
<td>pr(INB &gt; 0) (%)</td>
<td>1.52 (0.02)</td>
<td>21 (0.07)</td>
<td>64 (0.09)</td>
<td>68 (0.08)</td>
</tr>
<tr>
<td>K = €1,000</td>
<td>EVPI (€)</td>
<td>0 (0)</td>
<td>2.16 (0.07)</td>
<td>243 (0.94)</td>
</tr>
<tr>
<td>INB (€)</td>
<td>-7036 (2.55)</td>
<td>-3318 (2.42)</td>
<td>-655 (2.32)</td>
<td>141 (2.27)</td>
</tr>
<tr>
<td>pr(INB &gt; 0) (%)</td>
<td>0 (0.00)</td>
<td>0.52 (0.01)</td>
<td>30 (0.08)</td>
<td>54.65 (0.09)</td>
</tr>
<tr>
<td>K = €1,500</td>
<td>EVPI (€)</td>
<td>0 (0)</td>
<td>0.42 (0.04)</td>
<td>223 (1.09)</td>
</tr>
<tr>
<td>INB (€)</td>
<td>-12392 (3.73)</td>
<td>-6075 (3.60)</td>
<td>-1529 (3.47)</td>
<td>-12 (3.40)</td>
</tr>
<tr>
<td>pr(INB &gt; 0) (%)</td>
<td>0 (0)</td>
<td>0.08 (0.00)</td>
<td>20.89 (0.07)</td>
<td>49.85 (0.09)</td>
</tr>
</tbody>
</table>

pr(INB_K > 0) < 100%. For all unknown parameters (C_k, Y_k, p_eff, p_tp, and p_tp_eff), the EVSI values were lower than the corresponding EVPI. An example is given in Figure 7, where the expected value of sampling information on p_eff is shown for K = €500 and PCV = 44%; it increased from €300 for a sample size n = 5 to €340 for n = 100, €370 for n = 500, and up to the value of EVPI_{500} at n = 100,000.

**DISCUSSION**

The objective of this study was to introduce the techniques of cost-effectiveness analysis in veterinary medicine with an example in surgery for equine colic. Such techniques are important for the clinician working in equine colic referral centers who must present alternatives clearly to their clients. Indeed, colic is a very costly equine disease when surgery is required to avoid death. Studies reported 14% to 41% of horses referred for gastrointestinal colic at veterinary clinics required surgery. Colic is also costly because the percentage of surgically treated horses that survive varies with the pathophysiological mechanisms behind the colic syndrome, the physiological status of the animal, the study design and the time frame when surgery was performed.

Different indicators of survival after surgery have been proposed, among which is the preoperative PCV. Based on the
Belgian data, a clinician may recommend surgery when the horse’s PCV is below 44% because it is the threshold that best identified survivors and non-survivors, as given by the Youden index and the ROC (Figure 2). This comes at a cost because, in the Belgian study, 26% of the colic horses with PCV \leq 44\% died after surgery (0.26 \times 4,010 = 1,043) and 31% of the colic horses with PCV > 44\% survived after surgery (0.31 \times 19 = 5.9\, years). On the other hand, if surgery is performed on all colic horses without any preoperative testing, a loss of €1,520 (0.38 \times 4,000) will be incurred as a result of the surgery on non-survivors. Given these alternatives, the horse’s owner must make the final decision depending on how he/she valued the life-year of the horse. Because it quantifies and compares the economic efficiency of each alternative, cost-effectiveness analysis will help in making decisions that are consistent with maximizing the horse’s health gains given the existing information and the owner’s available resources.

**Baseline Analysis**

Given the parameters in Table 1, the strategy “test” is always less costly and less beneficial than the strategy “no test.” Indeed, in the “test” alternative, surgery is performed only on animals with a positive test, while in the “no test” alternative, surgery is performed on all horses. Because it is less beneficial than the “no test” alternative, the “test” alternative is said not to dominate and a judgment must be made whether the magnitude of its cost-saving is justified given its reduced effectiveness. This decision cannot be determined unless a cut-of-value, or maximal willingness-to-pay (K) for 1 life-year gained has been specified by the horse’s owner. Hence, the “test” strategy at PCV \leq 44\% is the most cost-effective when the horse’s owner is not willing to pay more than €672 for 1 life-year gained (to ensure INB\_K > 0). Note this value is much lower than the maintenance costs of a horse estimated at €1,500 per year. If the owner considered only maintenance costs, the surgery should always be performed because INB\_1,500 < 0.

**Analysis of the First Degree of Uncertainty**

Some variables may affect the selection of the best alternative, such as the surgery costs (C\_s), the probability of survival after surgery (p\_eff), and the number of life-years gained (Y\_e). Indeed, costs of colic surgery vary between veterinary clinics, horse value, colic etiology and localization, and existence or not of post-operative complications. In the USA, costs starts generally at $3,000, but can double for more difficult cases. Others reported costs varying from $4,500 to $7,500. In England, costs vary from £3,000 to £7,000, with £4,000 being the average. In France, a study has reported costs from €1,500 to €5,000. Postoperative survival rates fluctuate as well, with values at 21\%, 34\%, 54\%, 65\% and 69.7\%, up to 88\%. Period of survival after surgery is dependent upon the occurrence of postoperative complication. In a study of 341 horses that recovered from colic surgery, the probability of survival postoperatively decreased to 0.87 by 10 days, 0.82 by 100 days, and declined slowly to 0.75 at 600 days. In this study, all 3 variables affected the value of INB\_K at PCV = 44% but at different levels (Figure 3). Uncertainty on C\_s was the single most influential parameter as long as K was below €200, but this uncertainty would not alter the choice of the “test” alternative as the most cost-effective (INB\_K > 0 for all K). The influence of uncertainty on p\_eff and Y\_e increased with K, and for K > €200, uncertainty on p\_eff had the highest influence on the magnitude and the sign of INB\_K. There is a trade-off between the owner’s willingness to pay per extended life-year and the post-operative survival. If p\_eff is equivalent to the test positive predictive value (p\_tp\_eff), then the best alternative is to perform the test at any K value (INB\_K > 0 for all K). If the surgery is 100\% effective (p\_eff = 1), then the best alternative is not to perform the test, unless the owner is only willing to pay less than €130 per life-year (INB\_K < 0 for K > €130). Note the impact of uncertainty on the values of CS, Y\_e, and p\_eff on INB\_K is small in regards to the maintenance costs for a horse: at K = €1,500, INB\_K < 0 and the “no test” alternative.
is the most cost-effective (unless \( Y_E = 2 \) years or \( p_{tp\_eff} = p_{eff} \)).

**Analysis of the Second Degree of Uncertainty**

Prior distributions (Figure 4A) were used to describe the uncertainty on the base-values for \( C_S, Y_E, p_{tp, p_{eff}}, \) and \( p_{tp\_eff} \), uncertainty linked to the sampling variation. They were chosen compatible with published information on each unknown variables and conjugate to have prior and posterior distributions of the same family. This uncertainty is ricocheted in the spread of the posterior distributions of \( INB_k \) (Figure 4B) and the standard errors for the mean \( INB_k \) (Table 2). The distributions are widespread and the standard errors high, especially at high \( K \) values, making it difficult to draw conclusions or to make recommendations from the available information.

The CEAC are another popular graphical representation of uncertainty (Figure 5). In this study, the CEAC crossed the y-axis at 100%. This is the position at which the horse’s owner is unwilling to pay anything for health gain (\( K = 0 \)), in which case he/she should always choose the “test” alternative (given the current base-values). The point where the CEAC reaches equilibrium represents the position at which the horse’s owner is willing to pay an infinite amount for each additional gain in life-year. In this study, the equilibrium was at 0% because there was no more health gain in opting for the “test” alternative when \( K \) tended to infinity. Note that the CEAC is equal to \( 1 - \alpha \) (the 1-sided significance level) for testing the null hypothesis of a negative INB. For example, the null hypothesis is rejected at \( \alpha = 10\% \) for \( K < €320 \) because, as shown by the dotted line on Figure 5, the probability of obtaining \( INB_{320} > 0 \) is more than 90%.

**Value of Information Analysis**

To reduce the second order uncertainty observed in the baseline analysis, it would be desirable to realize specific research. The upper limit to the value of additional information is \( EVPI_k \). In this study, \( EVPI_k \) (Figure 6) was important for low values of \( K \), but became negligible as \( K \) increased. As a result, there is practically little purpose in further research to determine accurately the values of \( C_S, Y_E, p_{tp, p_{eff}}, \) and \( p_{tp\_eff} \) when the horse’s owner valued his/her horse at least at its maintenance costs (€1,500). The EVSI\(_k\) for \( p_{eff} \) is shown only as an illustrative purpose (Figure 7) because EVSI\(_k\) should always be lower than or equal to EVPI\(_k\). Indeed, EVSI\(_k\) is concerned with predicting the expected reduction in uncertainty resulting from the collection of data from an additional sample while EVPI\(_k\) is concerned with eliminating completely that uncertainty, and this can be achieved only by an infinitely large sample. By comparing the magnitude of EVSI\(_k\) to the costs of obtaining the sample, the optimum sample size for a further study on \( p_{eff} \) could be estimated. For example, the cost of collecting information on \( p_{eff} \) on 500 horses should be less than €0.6 per horse (EVSI\(_k\) = €300). Figure 7 shows also how EVSI increased with sample size and how even modest study sizes contribute substantially to the decision because of the relatively low precision in the base value for \( p_{eff} \).

**CONCLUSION**

In conclusion, comprehensive cost-effectiveness analysis provides an explicit, coherent, and flexible framework to help a decision maker in identifying the intervention with the greatest expected net benefit if he/she wishes to maximize health outcome subject to a budget constraint. By considering the expected value of information, he/she may also decide whether further research is required and to set priorities for collecting additional information. In our colic example, the base-analysis showed that a horse’s owner should prefer the “test” alternative for a horse with PCV = 44%, as long as he/she is willing to pay less than €672 each year the horse survives. However, due to sampling variation, he/she will make the wrong decision almost 50% of the time, as shown by the CEAC (Figure 5) and the posterior distributions of \( INB_{1,000} \) (Figure 4). At a willingness-to-pay of €500, the probability of postoperative survival was influencing most
the choice of the testing as the best alternative (Figure 3) but one should spent at most €381 (Table 2; EVPI$_{500}$) in research to reduce the second order uncertainty on the probability of survival. Finally, a study of postoperative survival of 500 colic horses would ensure an expected gain of €370 associated with a reduction in uncertainty.

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REFERENCES


