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.[1] Uncertainty on the model arises from 2 sources: model development and the values of the parameters.[2] 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_N) and cost (C_N) associated with the strategy "no test" were:

$$E_N = p\_eff \times Y_E$$

and

$$C_N = C_S, \text{ respectively.}$$

Figure 1. Decision tree displaying the alternatives of the horse colic problem.

For the strategy "test," effectiveness (E_T) and cost (C_T) were:

$$E_T = p\_tp \times p\_tp\_eff \times Y_E \text{ and}$$
$$C_T = (p\_tp \times C_S) + C_P, \text{ respectively.}$$

Baseline Analysis

For each proportion parameter (p_tp, p_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.[3] Base-values were obtained for C_S[4-8] and Y_E[9-13] after a search on Google and Medline on November 22, 2004 (Table 1). Then, values for the incremental net benefit (INB) were computed as:

$$INB_K = K \times (E_T - E_N) - (C_T - C_N),$$

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 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 INB_K. Maximum and minimum probabiliti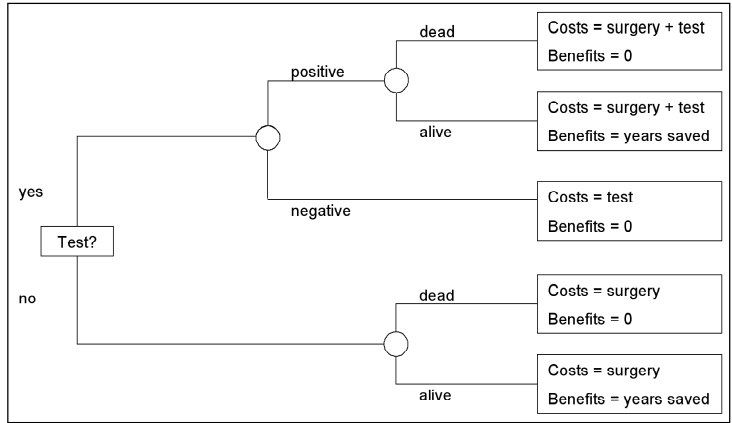es of survival after surgery were set at 100% and 50%, respectively. The cost of surgery varied from €1,500 to €7,500, and the length of survival after surgery ranged from 2 to 40 years (Table 1). The cost of PCV screening remained fixed at its current value of €10. Tornado diagrams depicted the effects of this type of uncertainty on 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_eff, p_tp, and p_tp_eff, prior distributions were Beta (α, β) 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.[14] The variables $\ln(C_S)$ and $\ln(Y_E)$ were each assumed to be a random sample from a Normal (μ, $1/\tau$) population with prior specifications $\mu \sim$ Normal (μ_0, $1/n_0\tau$) and $\tau \sim$ Gamma (η, δ), with $\eta = 4$ and $\delta = \eta\sigma^2_0$, $\mu_0 = \log$ (base-value) $- 1/2\sigma^2_0$, and $\sigma^2_0 = \log (1 + [\text{range}/(2 \times 1.98)])^2$, assuming 90% of the values for $\ln(C_S)$ and $\ln(Y_E)$ 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 η was obtained by trial and error. The prior distributions were chosen to compute explicitly the conjugated posterior distributions for INB_K.[15] Uncertainty intervals were estimated from the simulated data

Table 1. Parameters for the Colic Problem: Base Values for Baseline Analysis, Ranges for Analysis of First Degree of Uncertainty, and Distributions for Analysis of Second Degree of Uncertainty.

Parameter	Symbol	Base-Value	Range	Distribution
Surgery costs (€)	C_S	4,000	1,500 to 7,500	logN (4,000, 1,515²)
Test cost (€)	C_P	10		
Years of life extended after surgery	Y_E	19	2 to 40	logN (19, 5)
Proportion of horse surviving surgery (%)	p_eff	62	50 to 100	Beta (61, 99)
Proportion of horse with packed cell volume less than (%)	p_tp			
27%		2		Beta (2, 99)
32%		14		Beta (14, 99)
37%		35		Beta (35, 99)
44%		71		Beta (70, 99)
49%		83		Beta (82, 99)
52%		88		Beta (87, 99)
55%		95		Beta (94, 99)
61%		100		Beta (99, 99)
Proportion of surviving horse among those with packed cell volume less than	p_tp_eff			
27%		1.00		Beta (2, 2)
32%		0.79		Beta (11, 14)
37%		0.74		Beta (26, 35)
44%		0.74		Beta (52, 70)
49%		0.72		Beta (58, 82)
52%		0.69		Beta (60, 87)
55%		0.65		Beta (61, 94)
61%		0.62		Beta (61, 99)

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.[16] 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[17] was chosen to get EVPIK and EVSIK.[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 $Logn(\mu_0, 1/n_0\tau)$. 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,

$$EVPI_K = \check{E}(\max INB_K) - \max \check{E}(INB_K),$$
$$\text{and}$$
$$EVSI_K = \check{E}_D(\max INB_K) - \max \check{E}(INB_K),$$

where $\check{E}(\max INB_K)$ is the expected value under perfect information, $\max \check{E}(INB_K)$ is the expected value under current information, and $\check{E}_D$ is the expected value under imperfect information obtained from data D.
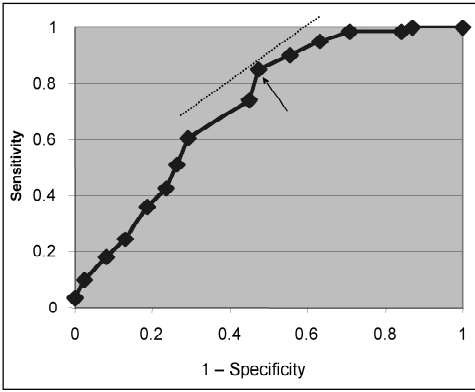
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Figure 2. The receiver characteristic curve for packed cell volume as an indicator of survival after surgery for equine colic. The arrow indicates the best cut-off for a packed cell volume of 44%.

RESULTS

In the study of Grulke et al,[3] 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%.[19] 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_E) 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 INB_1 = €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 INB_K decreased linearly as K increased and became negative for K > €672.
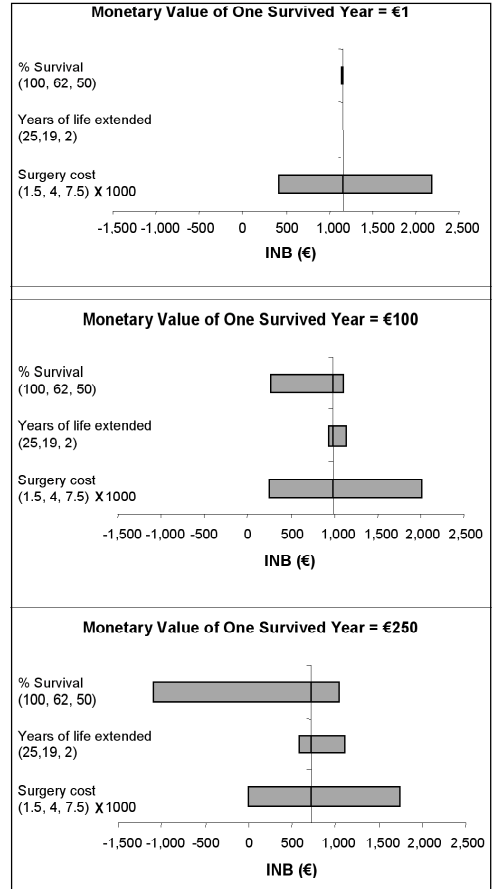

Figure 3. Tornado diagrams for the variation in incremental net benefit (INB) of the strategy "test" over the strategy "no test" given a maximum value for one survived year of €1, €100, and €250. The horizontal axis crossed the vertical axis at the base-value. Surgery costs varied from €1,500 to €7,500 with a base-value of €4,000; years of life extended after surgery varied from 2 to 25 years with a base-value of 19 years; and % of survival with a packed cell volume of 44% varied from 50% to 100%, with a base-value of 62%.

Analysis of the First Degree of Uncertainty

Uncertainty on surgery costs had highest effects on INB^1 for all PCV values (Figure 3). The INB^1 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
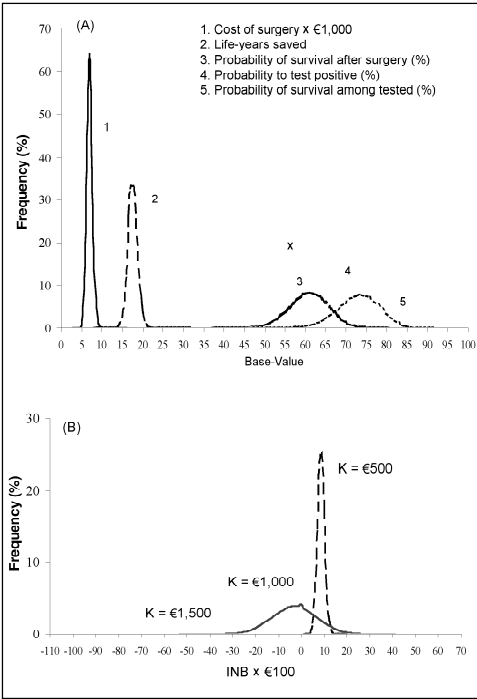
Figure 4. Prior distributions (A) for the parameters of the colic problem and posterior distributions (B) for incremental net benefit (INB) at various monetary values for 1 survived year (K) and for a packed cell volume of 44%.

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 $INB_{500} = -€1,093$ 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%, 44%, 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
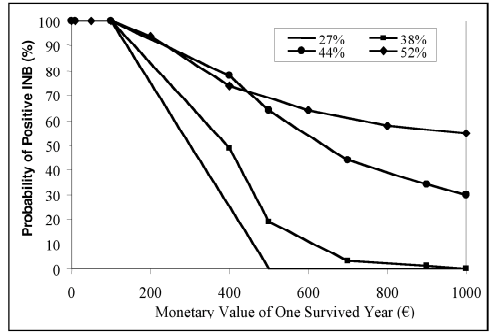

Figure 5. The cost-effectiveness acceptability curves for packed cell volume of 27%, 38%, 44%, and 52%, with incremental net benefit (INB) of the strategy "test" over the strategy "no test." The dotted line represents the 10% significance level for testing the null hypothesis of a negative INB.
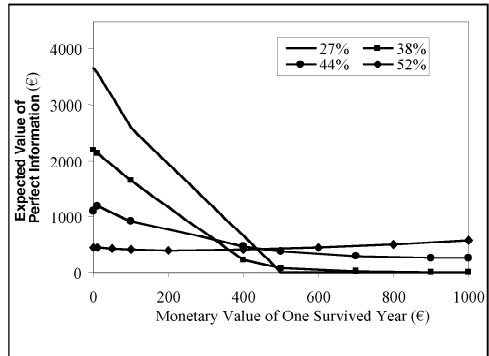

Figure 6. Expected value of perfect information for different monetary value of 1 survived year and for packed cell volume of 27%, 38%, 44%, and 52%.

showed that the probability of a positive INB_K was 100% for K ≤ €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 ≤ €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).

	PCV = 27%	PCV = 38%	PCV = 44%	PCV = 52%
K = €1				
EVPI (€)	3667 (0.76)	2189 (0.45)	1091 (0.23)	446 (0.09)
INB (€)	3667 (0.76)	2189 (0.45)	1091 (0.23)	446 (0.09)
pr(INB > 0) (%)	100 (0.00)	100 (0.00)	100 (0.00)	100 (0.00)
K = €100				
EVPI (€)	2606 (0.80)	1644 (0.51)	918 (0.32)	416 (0.24)
INB (€)	2606 (0.80)	1644 (0.51)	918 (0.32	416 (0.24)
pr(INB > 0) (%)	100 (0.00)	100 (0.00)	100 (0.00)	100 (0.00)
K = €500				
EVPI (€)	5.17 (0.11)	81 (0.40)	381 (0.81)	422 (0.83)
INB (€)	−1679 (1.43)	−561 (1.27)	219 (1.18)	293 (1.14)
pr(INB > 0) (%)	1.52 (0.02)	21 (0.07)	64 (0.09)	68 (0.08)
K = €1,000				
EVPI (€)	0 (0)	2.16 (0.07)	243 (0.94)	568 (1.41)
INB (€)	−7036 (2.55)	−3318 (2.42)	−655 (2.32)	141 (2.27)
pr(INB > 0) (%)	0 (0.00)	0.52 (0.01)	30 (0.08)	54.65 (0.09)
K = €1,500				
EVPI (€)	0 (0)	0.42 (0.04)	223 (1.09)	735 (1.98)
INB (€)	−12392 (3.73)	−6075 (3.60)	−1529 (3.47)	−12 (3.40)
pr(INB > 0) (%)	0 (0)	0.08 (0.00)	20.89 (0.07)	49.85 (0.09)

$\text{pr}(\text{INB}_K > 0) < 100\%$. For all unknown parameters (C_S, Y_E, 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.[20,21] Colic is also costly because the percentage of surgi-
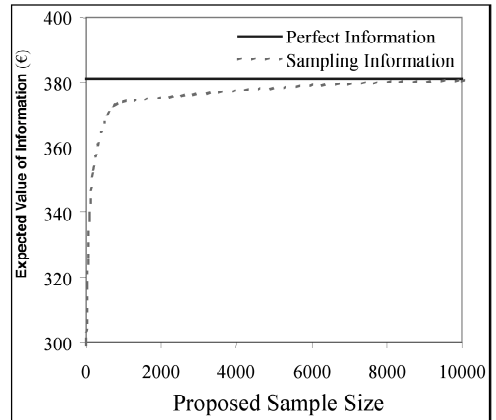

Figure 7. Expected values of perfect and sampling information on the probability of survival, assuming €500 for 1 survived year and a packed cell volume of 44%.

cally 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.[22]

Different indicators of survival after surgery have been proposed, among which is the preoperative PCV.[3,6,10,23] Based on the

Belgian data,[3] 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 ≤ 44% died after surgery (0.26 × €4,010 = €1,043) and 31% of the colic horses with PCV > 44% survived after surgery (0.31 × 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 × €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[24] 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.[25] Hence, the "test" strategy at PCV ≤ 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.[5,26] 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.[5] Others reported costs varying from €4,500 to €7,500.[4] In England, costs vary from €3,000 to €7,000, with €4,000 being the average.[7] In France, a study has reported costs from €1,500 to €5,000.[8] Postoperative survival rates fluctuate as well, with values at 21%,[9] 34%,[10] 54%,[12] 65%,[13] and 69.7%[11] up to 88%.[12] 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.[6] 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 ofthe "test" alternative as the most cost-effective ($INB_K > 0$ for all K). The influence of uncertainty on p_eff and Y_E increasedwith K, and for K > €200, uncertainty on p_eff had the highest influence on the magnitude and the sign of INB_K. There is atrade-off between the owner's willingness to pay per extended life-year and the post-operative survival. If p_eff isequivalent 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 heath 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 a = 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

1. Doubilet P, Weinstein MC, McNeil BJ: Use and misuse of the term "cost-effective" in medicine. *N Engl J Med* 1986;314:253–256.

2. Johnson-Masotti AP, Laud PW, Hoffmann RG, Hayat MJ, Pinkerton SD: Probabilistic cost-effectiveness analysis of HIV prevention: comparing a Bayesian approach with traditional deterministic sensitivity analysis. *Eval Rev* 2001;25:474–502.

3. Grulke S, Olle E, Detilleux J, Gangl M, Caudron I, Serteyn D: Determination of a gravity and shock score for prognosis in equine surgical colic. *J Vet Med A Physiol Pathol Clin Med* 2001;48:465–473.

4. Compton A, Hoffman A: *Should You Insure Your Horse?* Available at: http://www.petplace.netscape.com/articles/artShow.asp?artID=1207. 2004.

5. Freeman DW, Walker OL, Johnson BJ: "First time" horse ownership: selecting horses and budgeting horse interests. *Oklahoma Extension Fact Sheets* 2004;F-4004:1–4.

6. Proudman CJ, Smith JE, Edwards GB, French NP: Long-term survival of equine surgical colic cases. Part 1: patterns of mortality and morbidity. *Equine Vet J* 2002;34:432–437.

7. Royal Veterinary College of London: *Colic Fact Sheet*. Available at: http://www.rvc.ac.uk/Hospitals/SEH/Fact_Sheets/Colic.cfm. 2000.

8. Thoulon F: *Les Coliques*. Available at: http://users.skynet.be/bs715830/cavaliers/dos_col.htm. 2004.

9. Furr MO, Lessard P, White NA: Development of a colic severity score for predicting the outcome of equine colic. *Vet Surg* 1995;24:97–101.

10. McCarthy RN, Hutchins DR: Survival rates and post-operative complications after equine colic surgery. *Aust Vet J* 1988;65:40–43.

11. Puotunen-Reinert A, Huskamp B: Acute postoperative diarrhoea in colic horses. *J S Afr Vet Assoc* 1986;57:5–11.

12. van der Linden MA, Laffont CM, Sloet van Oldruitenborgh-Oosterbaan MM: Prognosis in equine medical and surgical colic. *J Vet Intern Med* 2003;17:343–348.

13. Wiemer P, Bergman HJ, van der Veen H, Pruissen L: Colic surgery in the horse: a retrospective study of 272 patients. *Tijdschr Diergeneeskd* 2002;15:682–686.

14. Vose D: *Quantitative Risk Analysis: A Guide to Monte Carlo Simulation Modelling*. John Wiley & Sons: New York; 1996.

15. Miconnet N, Cornu M, Beaufort A, Rosso L, Denis J-B: Uncertainty distribution associated with estimating a proportion in microbial risk assessment. *Risk Anal* 2005;25:39–48.

16. Stevens JW, O'Hagan A, Miller P: Case study in the Bayesian analysis of a cost-effectiveness trial in the evaluation of health care technologies: depression. *Pharm Stat* 2003;2:51–68.

17. Ades AE, Lu G, Claxton K: Expected value of sample information calculations in medical decision modeling. *Med Decis Making* 2004;24:207–227.

18. Tappenden P, Chilcott J, Eggington S, Oakley J, McCabe C: Methods for expected value of information analysis in complex health economic models: developments on the health economics of beta interferon and glatiramer acetate for multiple sclerosis. *Health Technol Assess* 2004;8:1–78.

19. Altman DG: *Practical Statistics for Medical Research*. Chapman and Hall: London; 1991.

21. Thoefner MB, Ersbøll AK, Jansson N, Hesselholt M: Diagnostic decision rule for support in clinical assessment of the need for surgical intervention with acute abdominal pain. *Can J Vet Res* 2003;67:20–29.

22. Kaneene JB, Miller R, Ross WA, Gallagher K, Marteniuk J, Rook J: Risk factors for colic in the Michigan (USA) equine population. *Prev Vet Med* 1997;30:23–36.

23. Thoefner MB, Ersbøll AK, Jensen AL, Hesselholt M: Factor analysis of the interrelationships between clinical variables in horses with colic. *Prev Vet Med* 2001;48:201–214.

24. O'Brien B, Drummond M, Labelle R, Willan A: In search of power and significance: issues in the design and analysis of stochastic cost-effectiveness studies in health care. *Med Care* 1994;32:150–163.

25. Karlsson G, Johannesson M: The decision rules of cost-effectiveness analysis. *Pharmacoeconomics* 1996;9:113–120.

26. Viaene J, Gellynck X, De Belder T: Het economisch beland van de paardensector. *Vakgroep Landbouweconomie in opdracht van de Belgische Confederatie van het Paard, Gent.* 2003.