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The economic value of information provided by milk biomarkers under different scenarios: Case-study of an ex-ante analysis of fat-to-protein ratio and fatty acid profile to detect subacute ruminal acidosis in dairy cows

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ABSTRACT

Monitoring systems (MS) provide additional information that many developers and researchers expect will reduce the uncertainty surrounding decision-making in livestock production and therefore enhance management decisions. However, the actual economic value of the information (VoI) yielded by MS has hardly been investigated. The aim of this study was to fill that void based on two objectives. The first is to estimate the VoI of MS prior to implementation using decision analysis based on scarce data from different sources. The second objective is to identify which factors most influence the VoI of MS and to develop recommendations about the focus of future MS development. To illustrate our objectives, we used a case study of two milk biomarkers used to monitor subacute ruminal acidosis (SARA) in dairy cows: fat-to-protein ratio (FPR) and the fatty acid profile (FAP). FPR is presently used to monitor SARA, while FAP is a newly developed test, currently in the pre-commercial phase, with reports of better accuracy than FPR. A stochastic decision tree model was used to estimate the expected monetary value of three levels of information with regards to SARA: (i) no monitoring, monitoring (ii) with FPR or (iii) with FAP. The VoI of FPR and FAP were calculated as the difference in expected monetary value of monitoring with FPR and FAP as compared with no monitoring, respectively. Several scenarios were modeled using sensitivity and elasticity analyses. The aim was not only to compensate for the scarcity of data for some variables, but also to identify under which conditions decisions based on FAP monitoring were indeed the best. In all the scenarios, monitoring SARA with FPR had the lowest expected monetary value. No monitoring was a better decision in 70% of the iterations in the scenario that described the most probable situation. The VoI of FAP was positive when SARA prevalence was between 0.21 and 0.79 with its maximum value at 0.61, when the treatment costs were lower than €116/case/year and when the disease costs were higher than €260/case/year. Moreover, an increase of specificity of the FAP to 0.95 yielded a positive VoI, whereas an increase of its sensitivity to 1.0 still yielded a negative VoI, suggesting that developers of the FAP should focus on improving its specificity rather than its sensitivity. To avoid suboptimal use of finite resources while developing MS, we recommend ex-ante investigation of the VoI of the MS under development.

1. Introduction

Monitoring systems (MS) measure health and production provide additional information. But to what extent does this information actually improve health management? Evaluating the value of information (VoI) derived from the use of MS is central to answering this question. The VoI is defined “as the expected utility with information minus the expected utility without information” (Kristensen, 2015, p. 229) that can be expressed in economic terms. Generally, a farmer will choose to invest in a MS if its associated benefits exceed its costs, thus deriving a high VoI and (higher) profitability (Russel and Bewley, 2013; Steeneveld et al., 2015). In a study of Kentucky (USA) dairy farmers, lack of knowledge on the economic value of MS represents a barrier to implementation (Russel and Bewley, 2013). Although numerous MS can monitor and detect different health and production issues (Zank and Schlatterer, 1998; Jorjong et al., 2014), only a few studies have

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investigated their profitability and value (Rutten et al., 2013; van der Voort et al., 2017). The paucity of studies may have several causes. First, according to Verstegen et al. (1995), the intangible nature of the benefits derived from the use of MS hampers their evaluation with traditional economic approaches such as cost-benefit analysis. Moreover, when benefits are tangible, one bottleneck may be the limited availability of economic methodologies that can investigate the VoI of MS (Verstegen et al., 1995) without bias. The research designs to estimate the VoI of MS are classified into positive and normative approaches (Verstegen et al., 1995) which are conducted ex-post and ex-ante, respectively. Selection bias is typically encountered in positive approaches. This is introduced when randomization of participants (e.g., farmers) cannot be ensured. For instance, participants may be better farm managers and, in turn, have better farm performance parameters than non-participants. Furthermore, problems of attribution might also arise if the size effect of the group using the MS is not compared to a control group. Accordingly, this approach disregards the fact that the observed differences in the group using the MS may be caused by other changes that were not controlled for by randomization. Both selection bias and the attribution problem are difficult to prevent without conducting experimental studies (Verstegen et al., 1995) that are typically expensive and sometimes impossible to perform. On the other hand, normative approaches rely heavily on prior knowledge of the economic impact caused by the health problem and by the possible interventions. The disease costs of ketosis (Raboisson et al., 2015; McArt et al., 2015; Liang et al., 2015; Mostert et al., 2017), other metabolic diseases (Kaneene and Hurd, 1990; van der Voort and Hogeveen, 2016) and costs of treatment of metabolic diseases (Fourichon et al., 2001) have been studied, but for other diseases both disease and treatment costs remain unknown (van der Voort et al., 2017). As a consequence, limited data availability becomes one of the main challenges when conducting a normative economic analysis of the VoI provided by MS (Steeneveld et al., 2015; van der Voort et al., 2017; Van De Gucht et al., 2018). In order to compensate for data scarcity, several alternatives can be used such as elasticity and sensitivity analyses (Bewley et al., 2010; Down et al., 2017), together with combining data from different available sources such as published literature and reports, expert opinion, and fitted distributions. For issues that are important and unexplored (such as the presented issue of the VoI of MS) Hardaker and Lien (2010) advocate the use of data from different resources instead of deviating the attention towards problems for which frequentist datasets are available.

Another reason for a small number of studies on the VoI of MS may be that the examined VoI of MS has been reported as being rather low and largely dependent on the accuracy of the MS in the reference situation (Jørgensen, 1993; van Asseldonk et al., 1999; Bewley et al., 2010; Jago et al., 2011; Kristensen et al., 2012; Giordano, 2014; Cha et al., 2016). As a result, researchers and developers may have had a hard time reconciling the low estimated VoI of MS as compared to their expectations (Bewley et al., 2010), and, as a consequence, they might have little interest in either estimating or reporting the VoI (Cornou and Kristensen, 2013). Nevertheless, many MS may still be of value to the decision-maker. Ex-ante studies can shed light on this value and its influencing factors. Hence, ex-ante assessment of the potential value of MS can help steer research and development towards aspects that can increase the value of MS.

Before embarking on further optimization of MS, developers must choose whether to focus on (i) improving its accuracy (e.g., whether it is more important to improve the sensitivity or specificity of the MS), (ii) identifying (or selecting) specific groups of animals at higher risk (i.e., higher prevalence), or (iii) improving knowledge about the costs of the condition being monitored (e.g., disease and treatment costs). This aspect has often been neglected in previous literature, with the exception of the studies by Bewley et al. (2010) and Van De Gucht et al. (2018). In the former study, the profitability of using an automatic body score system was assessed to guide researchers about goal-setting in light of finite research and development funds. A recent study had a similar goal and explored factors driving the economic value of automatic lameness detection systems in dairy cattle (Van De Gucht et al., 2018). Furthermore, ex-ante studies into the VoI can inform developers about the type and nature of the health and production problems for which a certain MS provides the most value.

The primary objective of this study is to present a method to quantify the VoI of MS using a decision analytical approach (Verstegen et al., 1995). To illustrate this objective we used a numerical example based on two diagnostic tests that detect subacute ruminal acidosis (SARA): (i) the fat-to-protein ratio (FPR) and (ii) the fatty acid profile (FAP). The former is currently used to detect SARA in Belgium (De Brabander et al., 2011) and the latter is in a pre-commercial phase; it has shown a similar sensitivity (Se) but a better specificity (Sp) than the FPR. The secondary objective is to provide insight into the factors influencing the VoI of the FAP, resulting in recommendations for the developers' focus when optimizing the MS in order to best allocate limited (capital, labor) resources.

2. Materials and methods

2.1. Procedure

Our procedure consisted of a stochastic decision tree simulation model applied to a typical Belgian specialized dairy farm. The stochastic decision tree simulates the impact of managing SARA, by means of the expected monetary value (EMV), using three potential decisions regarding its monitoring: (i) no monitoring at all, a strategy allowing herd-level decisions only; (ii) cow-level monitoring based on FPR; and (iii) cow-level monitoring based on FAP-based models. The latter two approaches imply that SARA treatment decisions are made at cow level, with the aim of maximizing herd-level economic performance. To estimate the VoI of MS we used the model framework suggested by Cornou and Kristensen (2013), where the VoI is estimated as the value of the decision based on the piece of information as compared to the value of the decision without having the information. The VoI of FAP and FPR were estimated as the difference between the EMV of the strategy to manage SARA based on monitoring results from FAP and FPR, respectively, minus the EMV of the strategy used to manage SARA without monitoring.

This stochastic decision tree simulation model was fed with data of the test characteristics of FAP and FPR, true prevalence (True Prev), disease costs (DC), and treatment costs (TC). Data on the costs of obtaining the additional information by using the biomarkers were not accounted for into our model and a value of €0 was inserted. This would provide insight into whether the biomarkers provided a value regardless of the cost of obtaining the extra information. In the situations in which the biomarkers had a value, this would represent the sensible upper limit that an economically rational farmer should pay to obtain the additional information. The data on the True Prev, DC and TC were scarce; we used the methodology proposed by Hardaker and Lien (2010) to address the evaluation of different potential decisions in situations of limited available data. In this case, Hardaker and Lien (2010) advocate the use of a combination of fitted distributions, data obtained from previous literature, and reports combined with expert judgement modeled as subjective probabilities. Data gathered from literature, consultation with experts, dairy cattle veterinarians, and feed advisors resulted in information on the True Prev of SARA, TC of SARA, and DC of SARA. In addition, several scenarios were simulated in sensitivity and elasticity analyses. We chose these analyses in accordance to other studies investigating the economic impact of MS (Bewley et al., 2010; Giordano, 2014) as this was reported as a way to account for the uncertainty of these data and to identify the combinations of variables that render FAP valuable.

The data used for the test characteristics of FAP and FPR originated from four previously conducted experiments, that aimed at identifying relevant milk fatty acids to diagnose SARA and reported the Se and Sp of the FPR (Colman et al., 2015) and the FAP (Colman, 2012). The ability of a diagnostic test to correctly diagnose positive and negative cases is defined by its Se and Sp, respectively.

The different components of the stochastic decision tree simulation model and data which served as input into our procedure are presented in detail below.

2.2. Test characteristics of FAP and FPR

To estimate the test characteristics of the milk biomarkers we used four datasets of four acidosis induction experiments in rumen-fistulated dairy cows (Colman et al., 2015). A brief description of the four datasets (1.1, 1.2, 2 and 4) can be found in Appendix A. To estimate the test characteristics of the FPR and the FAP, the ruminal pH was continuously measured. The datasets 1.1, 1.2, 2, and 4 were used to estimate the Se and Sp of the FPR (Colman et al., 2015). Datasets 1.1 and 1.2 were used to estimate the test characteristics of the FAP (Colman, 2012).

FPR was measured using Fourier Transformed-infrared spectroscopy. Eq. (1) presents a formula that estimates the normal FPR range for a cow in a specific season and in a specific lactation period (De Brabander et al., 2011).

$$\text{Normal FPR range} = \text{average FPR} + \text{Season Correction Factor} + \text{DIM Correction Factor} \pm 0.04 \quad (1)$$

Before the normal FPR range can be estimated, the average FPR for the last 12 months of one cow is required. Subsequently, the average FPR has to be corrected for the season and the lactation period. The season correction factor is +0.03 during the confined (inside the barn) period and −0.03 during the grazing period. The days in milk (DIM) correction factor is +0.05 if the cow has less than 100 DIM and −0.01 if the cow has more than 100 DIM. A correction factor of 0.04 is subtracted or added to take the individual variations between cows into account.

The estimated normal FPR range is subsequently compared to the measured FPR: if the measured FPR is lower than the lower limit of the normal FPR range, then the cow is diagnosed with SARA. Across the four datasets (datasets 1.1, 1.2, 2, and 4), FPR presented a Se of 0.72 and a Sp of 0.314 (Table 1).

In datasets 1.1 and 1.2 the milk FAP was identified and quantified by gas chromatography on a CP-Sil88 column for milk fatty acids (methyl esters) after extraction of the milk fat (Chouinard et al., 1997) and methylation (Stefanov et al., 2010). Colman et al. (2015) developed SARA classification models using support vector machine approaches which served as discrimination analysis to estimate the Se and Sp of the FAP in the two datasets. Depending on the dataset used, the FAP had a Se between 0.56 and 0.80 and its Sp was between 0.70 and 0.90 (Colman et al., 2015). Further, the receiving operating characteristics (ROC) curve with data of datasets 1.1 and 1.2 was used to determine the combination of plausible test characteristics of FAP (Fig. 1) (Colman, 2012). The ten different combinations of Se_{FAP} and Sp_{FAP} used in further analyses are indicated in Fig. 1. The combination of Se and Sp indicated by number 2, which had a Se of 0.64 and a Sp of 0.89, was used in the default scenario and the elasticity analyses (the details of these scenarios are provided in Section 2.7).

Table 1
Test characteristics of the fat-to-protein ratio (FPR) to diagnose subacute ruminal acidosis in the four datasets (1.1, 1.2, 2 and 4) from Colman et al. (2015).

Dataset	1.1	1.2	2	4	Weighted average
Number of observations	48	78	132	107	
Se $_{FPR}$ [a]	0.2000	1.00	0.8240	0.6210	0.7200
Sp $_{FPR}$ [b]	0.7080	0.1540	0.3780	0.1760	0.3143

[a] Sensitivity.
[b] Specificity.

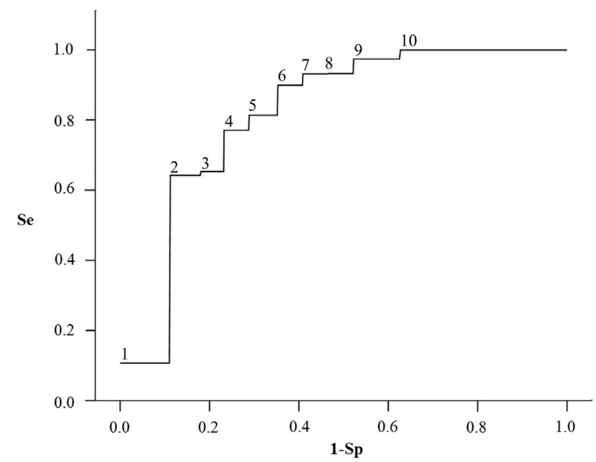

Fig. 1. Receiving operating characteristics curve of the fatty acid profile-based models to detect subacute ruminal acidosis of a combined dataset of datasets 1.1 and 1.2 (adapted from Colman, 2012). Point number 2[1] above the curve served as input data in the default scenario and elasticity analyses. All the 10 points[2] were used in the sensitivity analysis to explore whether the combination of sensitivity (Se) and specificity (Sp) of the fatty acid profile-based models yielded a positive economic value of information. [1] The number 2 displays the combination of sensitivity (Se) (0.64) and specificity (Sp) (0.89) used in the default scenario and the elasticity analyses. [2] The 10 numbers on the curve represent the 10 different combinations of Se and Sp for which the value of information of the fatty acid profile versus no monitoring was investigated in the sensitivity analysis. These combinations of Se and Sp are the following: 1: Se = 0.11, Sp = 1.00; 2: Se = 0.64, Sp = 0.89; 3: Se = 0.65, Sp = 0.82; 4: Se = 0.77, Sp = 0.77; 5: Se = 0.81, Sp = 0.71; 6: Se = 0.90, Sp = 0.65; 7: Se = 0.93, Sp = 0.59; 8: Se = 0.93, Sp = 0.54; 9: Se = 0.97, Sp = 0.48; 10: Se = 1.00, Sp = 0.37.

2.3. Disease costs of SARA

The DC incurred by cows with SARA is caused by decreased milk production, decreased efficiency of milk production, premature culling, and increased death rates (Krause and Oetzel, 2006). Similarly, Plaizier et al. (2009) report consequences such as lower feed intake, reduced fiber digestion, lower milk fat, diarrhea, laminitis, liver abscesses, increased production of bacterial endotoxins and inflammation characterized by increases in acute phase proteins. Although SARA occurs very frequently and has a high incidence in some herds, reports on the costs associated with SARA are scarce. Donovan (1997) stated that the costs of SARA in the dairy cow industry in the USA could be estimated between USD 500 million to USD 1 billion per year and the costs per affected cow (hereafter referred to as ‘cases’) was estimated as USD 1.12 per case/day or USD 409 per case/year. Stone (1999) demonstrated that SARA reduced milk production by 2.7 kg/day, milk fat production by 0.3% and milk protein production by 0.12%, resulting in direct costs of USD 400/case/year to USD 450/case/year. Similarly, Bipin et al. (2016) found a milk yield reduction of 2.8 l/day and a milk fat depression of 0.4% in dairy commercial herds in India. Formigoni (1998) estimated the cost of SARA in Italy to be approximately €260/case/year. According to an estimation performed by a dairy farm advisor in the Netherlands in a non-peer-reviewed publication (van Laarhoven, 2012) the presumable costs of SARA, including the indirect costs, totaled to €210/case/year which accounted for the increased indirect costs due to extra laminitis treatments (€10.50 to €24.50/case/year), milk losses due to lameness (8–15%), increased culling rate due to lame cows (4–20%), and costs for a longer calving interval (€0.70 to €1.67/case/year). van Laarhoven (2012) developed a farm-economic model to estimate the consequences of implementing measures to prevent SARA. The input data on the productivity was obtained from Dutch dairy farms that achieved a reduction in the prevalence of SARA from 23% to 5%. Because the estimation by van Laarhoven (2012) was the newest estimation, and the Dutch and Belgian dairy situations are similar, we assumed that the most probable value of DC of SARA in Belgium is €210/case/year. To account for the uncertainty of the limited data available in literature, we used a Pert distribution for the DC of SARA using @Risk (@Risk version 7.0, Palisade, Ithaca, NY, USA). The minimum value was set at €100/case/year, most probable value was inserted as €210/case/year and maximum was €450/case/year. Furthermore, we estimated the effect of the DC on the VoI of the FAP in the elasticity analysis-2 (characteristics of the parametrized model are described in Section 2.7).

2.4. Treatment costs of SARA

A range of dietary measures are taken to prevent or treat SARA: most common are a change of diet with or without supplementation with a buffer, reducing the amount of concentrate, and avoiding the supply of highly fermentable carbohydrates in the concentrate to increase the effective fiber in the ration. The use of buffers to prevent the appearance of SARA is used in highly productive herds in the USA (Hutjens, 1991; Enemark, 2009), and in Europe (De Letter, 2015; Moerman, 2015). However, the supplementation of buffers alone is not considered a long-term solution when not accompanied with optimization of the feeding management. These additional management measures may induce additional costs such as extra labor and/or reduced milk production (Enemark, 2009). To our knowledge, there are no reports of these indirect costs in literature. We therefore assumed that the TC were due to the supplementation of buffers and a change in the diet consisting of less concentrate and more forage. We also assumed that the treatment will be effective in 100% of the cases and that consequently, cows which received the buffer will be healthy after the treatment. This represents a best case scenario as complete recovery is not the case for all treatments (Zamarreño et al., 2003; Colman et al., 2010, 2012). For instance, the buffer treatment in combination with yeast and vitamin E did not have an effect on SARA occurrence in an experiment conducted by Colman et al. (2010) and only two out of three cows were cured when a buffer to treat SARA was used preventively (Colman et al., 2012). The results of our model therefore represent the upper limit of a best-case scenario.

Several commercial buffers are available on the market: sodium or potassium bicarbonate, sodium sesquicarbonate, sodium bentonite, calcium carbonate, carbonate of potassium. The first is the most commonly used in practice, with doses varying between 110 and 225 g/cow/day, and reported to positively affect milk production, fat percentage and dry matter intake (DMI) (Hutjens, 1991). A Belgian compound feed company producing and commercializing an additive with sodium bicarbonate advises administration of 250 g/cow/day (Kampf and Segers, 2015) as a standard ingredient in the ration which costs between €0.40/kg and €0.45/kg. These costs total to an average annual cost of €37 to €41/case/year. We assumed that the costs of reducing the amount of concentrate in the diet and increasing the forage as well as the additional labor involved will incur costs between €70 and €250/case/year. As no data were available and no one cost seemed more probable than another, we defined the TC as a uniform distribution with @risk in which the costs could range between €20 - €250/case/year. Similar to DC, the effect of TC on the VoI of FAP versus no monitoring was investigated in the elasticity analysis-3 (further detailed in Section 2.7).

2.5. True prevalence of SARA

Data on True Prev of SARA in commercial dairy herds were obtained from six previous studies (O'Grady et al., 2008; Kleen et al., 2009, 2013; Tajik et al., 2009; Kitkas et al., 2013; Stefańska et al., 2016). Table 2 details the number of herds used per study and their average prevalence and supplementary material-1 includes the prevalence per herd. These studies covered a considerable diversity of diets, ranging from Total

Table 2
Number of herds included and its average prevalence in each study used to fit the true prevalence of SARA.

Study	Number of herds	Mean Prev[a] (SD[b])
O'Grady et al. (2008)	12	0.1108 (0.0988)
Kleen et al. (2009)	18	0.1153 (0.1175)
Tajik et al. (2009)	10	0.2433 (0.1799)
Kitkas et al. (2013)	12	0.1581 (0.1579)
Kleen et al. (2013)	26	0.1992 (0.1641)
Stefańska et al. (2016)	9	0.1467 (0.1303)
Total	87	0.1636 (0.1522)

[a] Prevalence.
[b] Standard deviation.

Mixed Ration to grass silage, maize silage supplemented with concentrate, and grazing. In four studies the True Prev of SARA in a herd was estimated as the number of cows which had a ruminal pH lower or equal to 5.5 (measured in rumen fluid sampled between 3 and 6 h after feeding). The studies by Stefańska et al. (2016) and by Kleen et al. (2013) used a pH lower or equal to 5.6. The data on the True Prev of SARA served as a basis to fit a function with @Risk 7.5 distribution fitting feature (Palisade Corporation, Ithaca, NY, USA). We selected the function with the best fit based on their Akaike's Information Criteria (AIC) (i.e. the fit with a lowest AIC was chosen). The exponential function (Fig. 2) had the best fit (AIC = −134.86). Furthermore, to avoid the generation of unrealistic values of True Prev, such as negative values or values exceeding 1, the fitted distribution was truncated between 0 and 1. The average of the fitted True Prev was 0.1595 and the SD was 0.1567. The fitted function was fed into the decision tree as an input parameter.

2.6. Stochastic decision tree

Fig. 3 displays the decision tree used to perform the decision analysis in which the three possible decisions that the farmer can take regarding the monitoring of SARA are depicted: (i) no monitoring, (ii) monitoring based on FPR, (iii) monitoring based on FAP. The first fork, displaying the choice of no monitoring of SARA, consists of two secondary forks that depict the choice of treating and not treating the whole dairy herd. Each of the two secondary forks are followed by a chance node reflecting the proportion of healthy cows and those suffering from SARA. The latter proportion is defined by the True Prev of SARA and the former by 1 - True Prev. The number of cows with SARA and the number of healthy cows are calculated based on the total number of animals in the herd (N) and the True Prev of SARA (Eqs. (2) and (3), respectively).

$$\#\ \text{Cows with SARA} = N \times \text{True Prev} \tag{2}$$

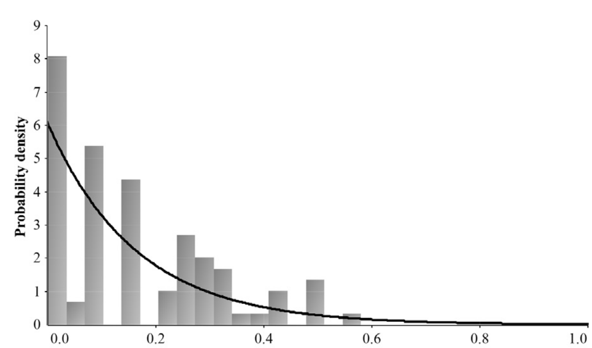

Fig. 2. Exponentially fitted function (black line) of the true prevalence of subacute ruminal acidosis of 87 herds as reported in literature[1] (grey bars). [1]O'Grady et al. (2008), Kleen et al. (2009), Tajik et al. (2009), Kitkas et al. (2013), Kleen et al. (2013), Stefańska et al. (2016).

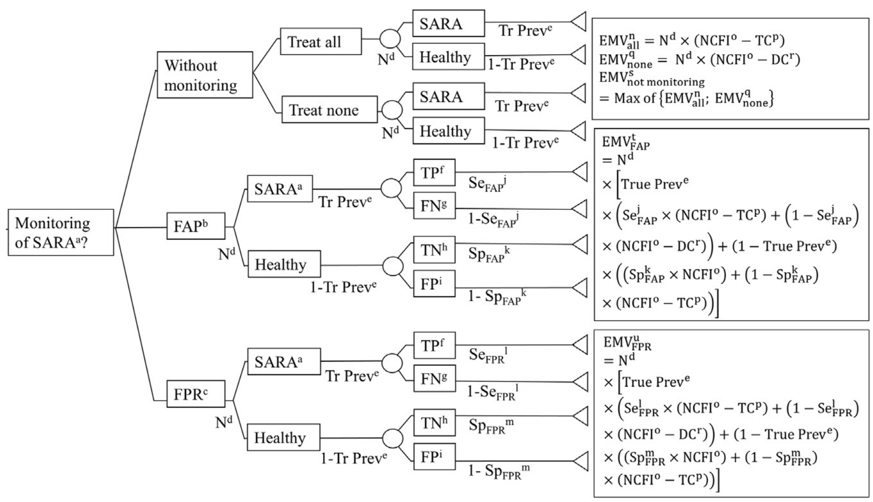

Fig. 3. Decision tree which depicts the three alternatives: i) no monitoring subacute ruminal acidosis (SARA), ii) monitoring SARA using the fatty acid profile (FAP), iii) monitoring SARA using the fat-to-protein ratio (FPR). [a] Subacute ruminal acidosis; [b] Fatty acid profile; [c] Fat-to-protein ratio; [d] Herd size; [e] True prevalence; [f] True positives; [g] False negatives; [h] True negatives; [i] False positives; [j] Sensitivity FAP; [k] Specificity FAP; [l] Sensitivity FPR; [m] Specificity FPR; [n] Expected monetary value of treating all in €/farm/year; [o] Net cash farm income in €/cow/year; [p] Treatment costs in €/cow/year; [q] Expected monetary value treating none in €/farm/year; [r] Disease costs in €/cow/year; [s] Expected monetary value of no monitoring SARA in €/farm/year; [t] Expected monetary value of using a FAP-based monitoring in €/farm/year; [u] Expected monetary value of using a FPR-based monitoring in €/farm/year.

$$\#\text{ Healthy cows} = N \times (1 - \text{True Prev}) \tag{3}$$

We assume that the farmer's decision to treat or not the herd – what we referred to as the 'no monitoring' decision – would depend on which decision entails the maximum EMV as described by Eq. (4).

$$EMV_{\text{no monitoring}} = \text{Max of}\{EMV_{\text{all}}; EMV_{\text{none}}\} \tag{4}$$

With EMV_{all} and EMV_{none} calculated as Eqs. (5) and (6), respectively, where NCFI is the net cash farm income and it is an indicator of the economic situation of the farm.[1]

$$EMV_{\text{all}} = N \times (NCFI - TC) \tag{5}$$

$$EMV_{\text{none}} = N \times (NCFI - \text{True Prev} \times DC) \tag{6}$$

The second and third decision forks outline the decision to use a milk biomarker to diagnose SARA. Both forks are followed by two chance branches reflecting the probability that a number of cows in the herd will either have SARA or be healthy. Likewise, each of the chance nodes is subdivided into two branches to reflect the imperfect test characteristics of the FAP and FPR, i.e. their Se and their Sp are not equal to 1. The branch displaying the cows with SARA consists of the proportion of true positives (TP), i.e. the proportion of cows which is correctly detected as positive by the biomarker and has SARA, and of the proportion of false negatives (FN), i.e. the proportion of cows which is detected as "healthy" by the biomarker but is actually suffering from SARA.

Similarly, the chance fork which stems from the healthy cows consists of the proportion of true negatives (TN), i.e. the proportion of cows detected as negative by the milk biomarker and are healthy, and the proportion of false positives (FP), i.e. the proportion of cows detected as positive by the biomarker but are healthy.

We used the framework of Cornou and Kristensen (2013) to estimate the VoI of FAP and FPR. This framework accounts for how the information is translated into action by the farmer. In the present study, farmers were assumed to respond to the new information provided by the biomarkers using a representative heuristic. This applies more weight to the new information than to the previous information available (e.g., the farmer's suspicion of the existence of SARA based on prior knowledge). When faced with the monitoring results, a dairy manager who uses a representative heuristic will treat the cows accordingly, thus neglecting previous information. In other words, each cow that tests positive according to the biomarker is treated, and cows that test negative will remain untreated. Therefore, cows with positive results (TP and FP) will lead to TC. Cows with FN results are not treated, leading to a case of SARA, which incurs DC. Cows with TN test results are healthy and are therefore not treated for SARA, thus incurring no costs. The EMV of treating only animals that receive a positive result according to FPR or FAP is described in the following formula (Eq. (7)).

$$\begin{aligned} EMV_{\text{biomarkers}} = N \times [&\text{True Prev} \times (Se \times (NCFI - TC) \\ &+ (1 - Se) \times (NCFI - DC)) + (1 - \text{True Prev}) \\ &\times ((Sp \times NCFI) + (1 - Sp) \times (NCFI - TC))] \end{aligned} \tag{7}$$

The VoI of the FAP versus no monitoring and the VoI of the FPR versus no monitoring were estimated with Eqs. (8) and (9), respectively.

$$VoI_{\text{FAP versus no monitoring}} = EMV_{\text{FAP}} - EMV_{\text{no monitoring}} \tag{8}$$

$$VoI_{\text{FPR versus no monitoring}} = EMV_{\text{FPR}} - EMV_{\text{no monitoring}} \tag{9}$$

2.7. Default scenario, elasticity, and sensitivity analysis

To account for the uncertainty of our input parameters and to investigate under which conditions the FAP-based models are of value, we simulated different scenarios. The different scenarios simulated are described in Table 3.

The stochastic simulations were performed in @Risk 7.5 (Palisade Corporation, Ithaca, NY, USA). Latin Hypercube sampling was used with a fixed seeder of 1 to ensure all simulations provided repeatable results. For all the scenarios 10,000 iterations were ran.

For all the scenarios, cumulative distribution functions (CDF) were plotted for the EMV[2] of the three decisions: (i) no monitoring, (ii) monitoring with FPR, (iii) monitoring with FAP. Furthermore, the EMV of the three modeled decisions were evaluated applying a stochastic efficiency method called first-degree stochastic dominance (Hardaker et al., 1997). This technique is used to assess which decision is preferred and it is based on the assumption that the decision maker will prefer 'more' rather than 'less'. First-degree stochastic dominance is based on relationships between the CDF of alternative decisions. Let's imagine two decisions: (i) decision A and (ii) decision B. They are described by CDF EMV_A and CDF EMV_B, respectively. The decision A dominates decision B by first-degree if graphically the CDF of the EMV_A lies always below and to the right of the CDF of the EMV_B (Hardaker et al., 1997).

[1] The NCFI consists of the total receipts minus the total expenses. Total receipts consists of the financial gains received by the different activities performed by the specialized dairy farm such as crop (e.g. wheat, barley, etc.) and dairy (milk, cull cows, calves, etc.) as well as government payments.

[2] A CDF of EMV at value x is the probability that the EMV takes a value less than or equal to x. The values of the EMV are displayed on the horizontal axis. Because the vertical axis represents a probability, its values lie between 0 and 1. The vertical axis increases from 0 to 1 as the EMV values increase on the horizontal axis.

Table 3
Description of the different scenarios modeled to account for the uncertainty of the input data.

Name of the analysis	Varying variables	Fixed variables
Default scenario	DC[a] (€/case/year) ~ Pert distribution (100, 210, 400) TC[b] (€/case/year) ~ Uniform distribution (20, 250) True Prev[c] ~ fitted as an exponential distribution with mean 0.1595	Se $_{FAP}$[d] = 0.6421 Sp $_{FAP}$[e] = 0.8877 N[f] = 95[g] NCFI[h] = €1,277/cow/year[g] Se $_{FPR}$[i] = 0.72 Sp $_{FPR}$[j] = 0.3143
Elasticity analysis −1	True Prev[c] ~ Uniform distribution (0,1)	DC[a] (€/case/year) = 223.33 TC[b](€/case/year) = 135 Se $_{FAP}$[d] = 0.6421 Sp $_{FAP}$[e] = 0.8877 N[f] = 95[g] NCFI[h] = €1,277/cow/year[g]
Elasticity analysis − 2	DC[a] (€/case/year) ~ Uniform distribution (100, 400)	TC[b] (€/case/year) = 135 True Prev[c] = 0.1595 Se $_{FAP}$[d] = 0.6421 Sp $_{FAP}$[e] = 0.8877 N[f] = 95[g] NCFI[h] = €1,277/cow/year[a]
Elasticity analysis − 3	TC[b] (€/case/year) ~ Uniform distribution (20, 250)	DC[a] (€/case/year) = 223.33 True Prev[c] = 0.1595 Se $_{FAP}$[d] = 0.6421 Sp $_{FAP}$[e] = 0.8877 N[f] = 95[g] NCFI[h] = €1,277/cow/year[g]
Sensitivity analysis − 1	Se $_{FAP}$[d] increased from 0.6421 to 0.66 and onwards by 0.02 intervals until 1 DC[a] (€/case/year) ~ Pert distribution (100, 210, 400) TC[b] (€/case/year) ~ Uniform distribution (20, 250) True Prev[c] ~ fitted as an exponential distribution with mean 0.1595	Sp $_{FAP}$[e] = 0.8877 N[f] = 95[g] NCFI[h] = €1,277/cow/year[g]
Sensitivity analysis − 2	Sp $_{FAP}$[e] increased from 0.8877 to 0.90 and increased onwards by 0.02 intervals until 1 DC[a] (€/case/year) ~ Pert distribution (100, 210, 400) TC[b] (€/case/year) ~ Uniform distribution (20, 250) True Prev[c] ~ fitted as an exponential distribution with mean 0.1595	Se $_{FAP}$[d] = 0.6421 N[f] = 95[g] NCFI[h] = €1,277/cow/year[g]
Evaluation of VoI[k] FAP versus no monitoring on ROC[l] points of Fig. 1	10 discrete combinations of Se $_{FAP}$[d] and Sp $_{FAP}$[e] (Fig. 1) DC[a] (€/case/year) ~ Pert distribution (100, 210, 400) TC[b] (€/case/year) ~ Uniform distribution (20, 250) True Prev[c] ~ fitted as an exponential distribution with mean 0.1595	N[f] = 95[g] NCFI[h] = €1,277/cow/year[g]

[a] Disease costs.
[b] Treatment costs.
[c] True prevalence.
[d] Sensitivity of the fatty acid profile.
[e] Specificity of the fatty acid profile.
[f] Herd size.
[g] Hemme (2016)
[h] Net cash farm income.
[i] Sensitivity of the fat-to-protein ratio.
[j] Specificity of the fat-to-protein ratio.
[k] Value of information.
[l] Receiving Operating Characteristics Curve.

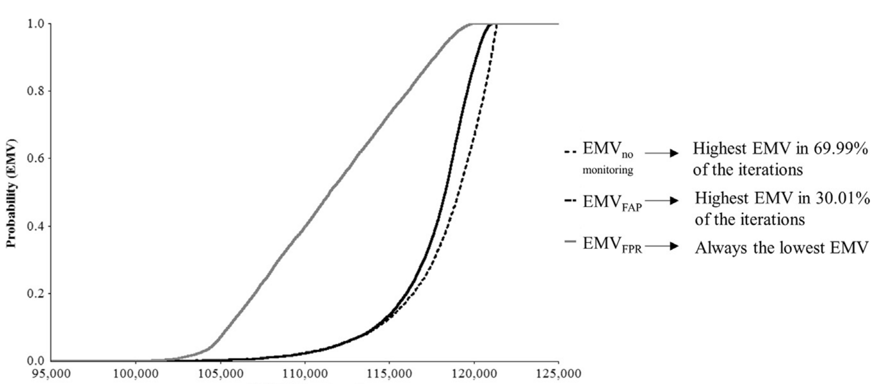

Fig. 4. Continuous cumulative distribution functions of the expected monetary value (EMV) in €/farm/year of (i) no monitoring subacute ruminal acidosis (SARA) (dotted black line), (ii) monitoring SARA using fatty acid profile (FAP) (solid black line), (iii) monitoring SARA using fat-to-protein ratio (FPR) (grey line) in the default scenario[1.] [1] Under the default scenario the different input variables were parametrized as follows: the disease costs (€/case/year) as RiskPert (100, 210, 400), the treatment costs (€/case/year) as RiskUniform (20, 250) and true prevalence of SARA as a fitted exponential distribution with mean 0.1595. The test characteristics of the fatty acid profile and the fat-to-protein ratio were: sensitivity (Se) = 0.64 and specificity (Sp) = 0.89 and Se = 0.72 and Sp = 0.31, respectively. The parameterized herd size was 95. The net cash farm income was kept as €1,277/cow/year.

3. Results

3.1. Default scenario

Fig. 4 presents the CDF of the EMV of the three possible decisions in the default scenario: (i) no monitoring, (ii) monitoring with FPR, (iii) monitoring with FAP. No monitoring yielded a higher EMV than making treatment decisions based on the FAP in 69.99% of the simulations (data not shown). Furthermore, in approximately 96% of these iterations it was better to treat none of the cows (data not shown). This was mainly a consequence of the low True Prev (on average 0.1595, Fig. 2) in combination with the modeled TC and DC (see Table 3 for the input parameters modeled) that made the FAP biomarker of no value to detect SARA.

As seen in Fig. 4, the functions of the EMV of both strategies, i.e. no monitoring SARA (dotted black line) and monitoring SARA by means of the FAP (solid black line) lie graphically to the right and below of the monitoring based on the FPR (grey line). As a consequence, no monitoring and monitoring with FAP had first-degree stochastic dominance over SARA treatment decisions based on monitoring with FPR. In other words, the SARA treatment decisions based on FPR always led to the lowest EMV compared to the other two decisions modeled. Treatment decisions of SARA based on FAP always outperformed those made by FPR, which was related to the low test performance of the latter (Se = 0.72 and Sp = 0.31) compared to the FAP–based models (Se = 0.64 and Sp = 0.89). This phenomenon occurred for all the simulated elasticity and sensitivity analyses presented below (data not shown). Furthermore, because the EMV_{FPR} was always the lowest of the three decisions, the VoI of FPR is not discussed here.

3.2. Elasticity and sensitivity analyses

The results of the elasticity analysis-1 are portrayed in Fig. 5. At average TC of €135/case/year and most likely DC of €223.33/case/year, using FAP to detect SARA had a positive value for a True Prev between 0.21 and 0.79 (maximum of 0.61). Outside this range, the VoI of FAP was negative (Fig. 5).

The elasticity analysis-2 shows the effect of DC in the VoI of FAP versus no monitoring (Fig. 6a). At average TC of €135/case/year and most likely True Prev (0.1595), the VoI of FAP increased with DC and became positive at a DC of €259.44/case/year (Fig. 6a).

Elasticity analysis-3 shows the influence of the TC, given the most likely DC (€223.33/case/year) and most likely True Prev (0.1595), on the VoI of FAP (Fig. 6b). This figure displays an apparently counter-intuitive shape because the VoI of FAP increases when the TC increase between €20 and €35.62/case/year. In this range of TC, the EMV_{FAP} was higher than the $EMV_{no\ monitoring}$ corresponding to the decision to treat all cows. As described in Eqs. (5) and (7), both the EMV_{all} and EMV_{FAP} decreased as the TC increased. Nevertheless, given that the EMV_{all} is directly affected by the TC, when the TC increased, the EMV_{all} decreased faster (€95 per additional €1 of TC) than the EMV_{FAP} (€18.70 per additional €1 of TC). In the latter scenario, the TC are influenced by the Se_{FAP}, Sp_{FAP} and True Prev, reducing the effect of the increase of the TC (Eq. (7)). In the first part of Fig. 6b, the VoI of the FAP is estimated as the EMV_{FAP} minus the EMV_{all} and the latter is smaller than the former. This explains why the VoI of FAP increased when the TC increased. In the second part, from TC of €35.62/case/year onwards, the VoI of FAP versus no monitoring decreased and reached negative values when the TC were €116.22/case/year. In this part the highest EMV of the decision 'no monitoring' was found when none of the cows were treated, which is independent of the TC (Eq. (6)) and constant at €117,931/farm/year. This value is reached by the EMV_{FAP} when the TC are above €116.22/case/year. From this value onwards the decision with the highest EMV is to treat none of the cows instead of using the FAP to make SARA treatment decisions.

Fig. 5. Results of the elasticity analysis-1[1] which show the effect of true prevalence of subacute ruminal acidosis (SARA) on the value of information (VoI) of the fatty acid profile (FAP) to detect SARA versus no monitoring. [1]In the elasticity analysis-1 the disease costs and treatment costs were kept at their most probable deterministic values that were €223.33/case/year and €135/case/year, respectively. The sensitivity and specificity of the fatty acid profile were kept as 0.64 and 0.89, respectively. The herd size was kept as 95 and the net cash farm income as €1,277/cow/year.

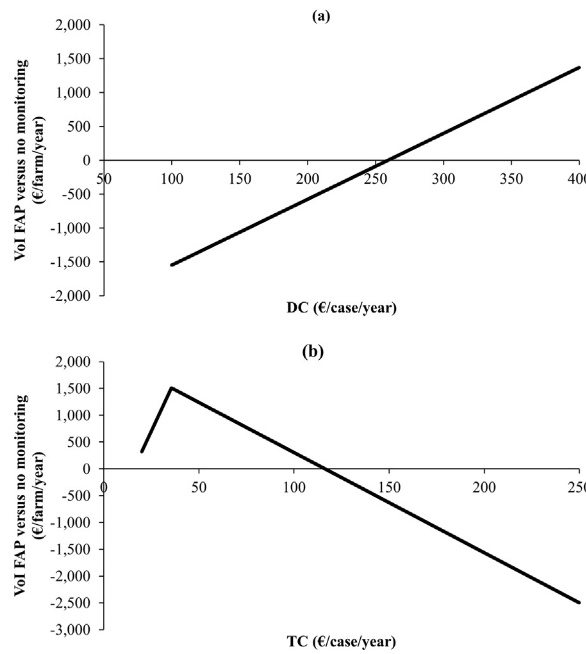

Fig. 6. Results of the elasticity analyses-2[1] and − 3[2] which present the effect of the disease costs (DC) (a) and treatment costs (TC) (b) on the value of information (VoI) of fatty acid profile (FAP) to detect subacute ruminal acidosis versus no monitoring. [1]In elasticity analysis-2, the effect of the DC on the VoI of the FAP was estimated by accounting the DC as a uniform distribution (Riskuniform (100,400)) while keeping the TC at €135/case/year, the true prevalence at 0.16, the sensitivity of the FAP and the specificity of the FAP at 0.64 and 0.89, respectively, the herd size at 95 and the net cash farm income at €1,277/cow/year. [2] In the elasticity analysis-3 the effect of the TC on the VoI of the FAP was estimated by accounting the TC as a uniform distribution (Riskuniform (20,250)) and the DC at €233.33/case/year, and the rest of the variables remained as in the elasticity analysis-2.

Fig. 7a shows the results of the sensitivity analysis-1. Under the input parameters defining the default scenario (Table 3), the VoI of FAP versus no monitoring always remained negative even when Se of FAP could be improved up to 1.00 with the same Sp (0.89). Contrastingly, if the Sp would increase up to 0.95 with the same Se (0.64), the VoI of FAP would become positive. If the Sp could be improved up to 1 while maintaining the same Se, the VoI of FAP versus no monitoring will be on average €543/farm/year (Fig. 7b).

The results of investigating the VoI of FAP at 10 different points of the ROC curve of Fig. 1 demonstrated that under all the possible current combinations of Se and Sp, the VoI remained negative (Fig. 7c). Moreover, under the default scenario, a higher the Se associated with a

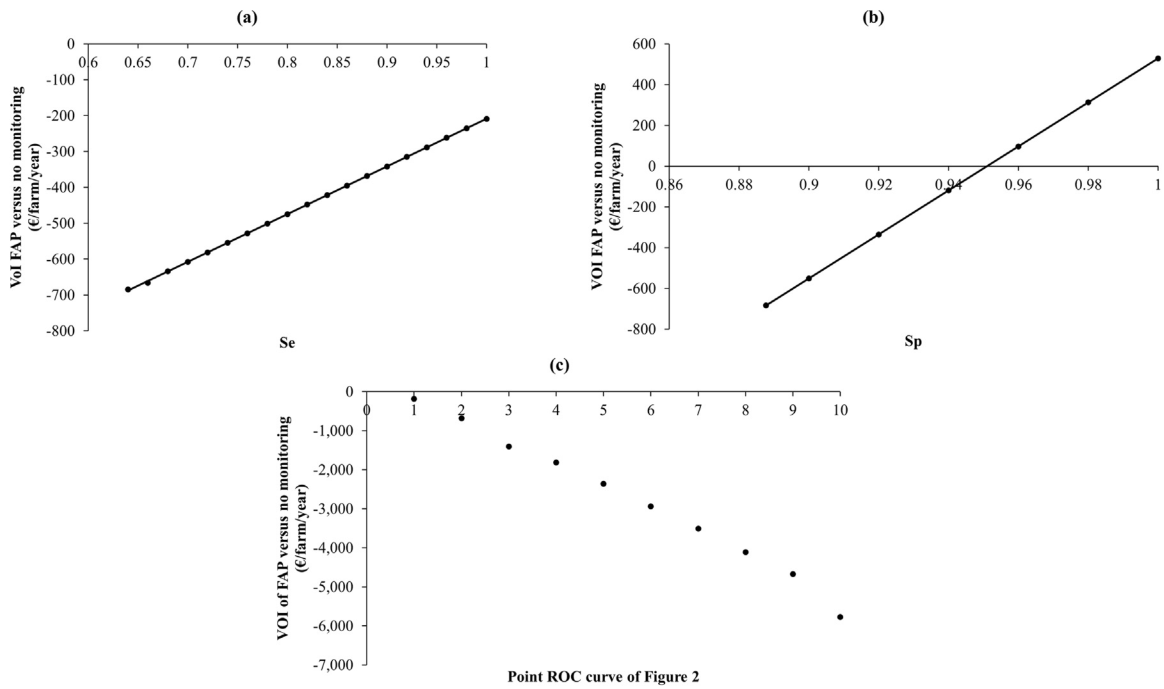

Fig. 7. Results of the sensitivity analysis-1[1] (a), sensitivity analysis-2[2] (b) and of the discrete analysis of the 10 different combinations of sensitivity (Se) and specificity (Sp) of fatty acid profile (FAP) to monitor subacute ruminal acidosis[3] (c). [1]In the sensitivity analysis-1 all variables were kept as in the default scenario and the sensitivity of the FAP was increased by intervals of 0.02 until sensitivity reached 1. [2] In the sensitivity analysis-2 all variables were kept as in the default scenario and the specificity of the FAP was increased by intervals of 0.02 until specificity reached 1. [3] The 10 combinations of sensitivity and specificity of the fatty acid profile (FAP) used to estimate the value of information of FAP versus no monitoring are displayed in the receiving operating characteristics (ROC) curve of the FAP-based models in Fig. 1, all the other variables remained as in the default scenario.

lower the Sp of FAP always resulted in a reduction of the VoI.

4. Discussion

The VoI provided by FAP was negative in the default scenario (Fig. 4). In other words, using the modeled input parameters of this scenario, which involved large intervals, the EMV of no monitoring SARA and making herd-level decisions was higher than the EMV of using the FAP to detect SARA to treat individual cows. To our knowledge this is the first study that attempts to estimate the VoI of milk biomarkers to monitor SARA. Therefore, we were unable to compare our results with existing literature. Nevertheless, our outcome coincides with the rather low VoI obtained for different Precision Agriculture (Bennett and Pannell, 1998; O'Connell et al., 1999; Pannell and Glenn, 2000) and Precision Livestock MS (Jørgensen, 1993; van Asseldonk et al., 1999; Bewley et al., 2010; Jago et al., 2011; Giordano, 2014; Cha et al., 2016; Down et al., 2017). In these studies, informed decisions based on additional information do not always result in better decisions made as compared to no monitoring. Cha et al. (2016) revealed that the value of pathogen specific information in treating clinical mastitis in dairy cows was rather low. In contrast, the highest VoI was derived when the farmer assumed that the pathogen causing the clinical mastitis was the one with the highest incidence in the herd and no pathogen-specific information was obtained. The profitability of an estrus detector for dairy cows was investigated by van Asseldonk et al. (1999). In the best case scenario, when the detection rate was improved from 50% to 90% at first insemination, and assuming a conception rate of 40% and the yearly fat protein corrected milk production was 7,580 kg/cow/year, the benefit entailed through the detector was only €0.58 per 100 kg fat protein corrected milk per year (van Asseldonk et al., 1999). Moreover, the detection rate did not show a linear relationship with gross margin, which was highly dependent on the conception rate and the milk production. In fact, the higher the reference conception rate and milk production, the lower the additional benefits resulting from an improved estrus detection (van Asseldonk et al., 1999). Their results were confirmed by several recent studies demonstrating that, on average, the use of automatic estrus detection sensors yielded rather low benefits which were highly dependent on the performance of the reference method in place (Jago et al., 2011; Giordano, 2014). In addition, Giordano (2014) revealed that the benefits attained were sometimes lower than the costs of implementing the MS. Furthermore, Jørgensen (1993) found that the benefits accrued could barely cover the costs of individual identification tags when precise pig weighing was used as compared to batch delivery of pigs.

The benefits of MS are scenario specific (Bewley et al., 2010; Jago et al., 2011; Giordano, 2014). These studies have explored several scenarios to better understand the circumstances in which the investigated MS were beneficial for the farmer. Similarly, in our study sensitivity and elasticity analyses were conducted to gain insights into the conditions under which the monitoring with FAP would enhance SARA treatment decision making. The FAP showed a positive VoI (i) for (sub-)herds in which the True Prev of SARA is medium to high (Fig. 5), and (ii) when treating SARA can lead to more than marginal improvements in economic performance per cow, i.e. when TC are lower than €116/case/year (Fig. 6(a)) or when DC are higher than €260/case/year (Fig. 6(b)), and when the Sp of the test would be improved up to 0.95 while maintaining the same Se (Fig. 7(b)). When one or more of these conditions are not met, the window in which the FAP is of economic value narrows. Under medium prevalence levels of SARA, the use of FAP to detect SARA does not improve farm's economic performance. Therefore, implementation of the FAP milk biomarkers could be profitable in a herd with a higher prevalence than an average herd, as the economic value rose when prevalence increased to medium levels. Our results suggest that making SARA treatment decisions by means of FAP monitoring would be profitable for the 32 out of the 87 herds from previous studies used to fit the True Prev distribution with a prevalence of SARA between 0.21 and 0.58 (Supplementary material-1) (Fig. 5). Alternatively, it could be profitable to use the FAP milk biomarker in subgroups of a herd that are at a higher risk of developing SARA such as cows which are between 15 and 30 days in milk with individual compound feeding, which is rapidly built up during this period. As we did not account for the additional costs of obtaining the information, these positive values represent the maximum amount that the farmer could reasonably pay, from an economic perspective, for the additional information without incurring losses. This only holds true, however, when the use of the FAP biomarker entails no fixed investment or implementation costs, and hence only implies a variable cost when it is used. Our results are upper limit estimates as we assumed that the treatment (combination of buffer and adaptation of the diet) will yield an immediate 100% cure rate, which is not always the case (Colman et al., 2010, 2012). In the future, this conclusion could potentially be nuanced if new research can decrease the uncertainty associated with the treatment and disease costs. The potential value may also depend on market conditions. For instance when milk prices are high and feed prices are low, it is likely that the difference between DC and TC becomes larger, so that the economic VoI of biomarkers to detect SARA would increase.

In all the simulated scenarios, the use of the FPR biomarkers to decide on SARA treatment led to a decrease in farm profitability (Fig. 4 for default scenario; data for the other scenarios are not shown but are available upon request). The performance of FPR-based models to diagnose SARA is quite poor (Guegan et al., 2015), resulting in first-degree stochastic dominance by both of the alternative decisions: (i) no monitoring and (ii) FAP-based monitoring (Fig. 4). This might explain why farmers who have an automatic milking system with an incorporated MS to measure FPR do not use it often or do not request it regularly from the provider (Steeneveld and Hogeveen, 2015). Moreover, French organic dairy farmers showed a very low acceptance of the difference between the milk fat and milk protein content levels (i.e. a proxy for the FPR used in Belgium) as an indicator of prevalence of SARA and Swedish farmers have rejected this indicator altogether (Duval et al., 2016). Given that the FAP-based models have shown a better performance than the FPR, it suggests that the FAP will be a better monitoring tool, when it becomes commercially available, to detect SARA than the FPR.

From an animal health and welfare point of view, both veterinarians and MS researchers wish to avoid false negatives, thus a high Se is desired. However, in our study, under the default scenario, we showed that even when the Se of the FAP was improved up to 1.00, the decision of no monitoring SARA in the herd remained the decision with the highest EMV (Fig. 7a). Given the low prevalence of SARA (Fig. 2), we demonstrated further that from an economic perspective, attempts to improve Sp are the most interesting. If Sp was increased up to 1.00, the use of FAP to monitor SARA would become profitable (Fig. 7b). Accordingly, the FAP needed to have a Sp higher than 0.95 maintaining the same Se of 0.64 to achieve a positive VoI. These results are in line with the desires of farmers, as they prefer to have as few false alarms as possible and therefore a MS with a high Sp (Claycomb et al., 2009; Kamphuis et al., 2010; Mollenhorst et al., 2012). Given the plausible combinations of Se and Sp of FAP, the VoI of the current FAP-based models always remains negative (Fig. 7c). Improvement of both the Se and Sp of an MS would require a large amount of time, money, and resources. We therefore advocate that an ex-ante evaluation of improvement of the test characteristics is performed first, as done in the current study in order to guide MS developers to optimize the allocation of finite resources.

The data scarcity of the input parameters (TC, DC, True Prev) to evaluate the EMV of the three potential decisions to monitor and treat SARA is a limitation of this study. In particular, the data on TC and DC were very scant. The economic impact of dairy metabolic diseases has been neglected in the literature (Raboisson et al., 2015; Van der Voort et al., 2017), but obtaining accurate estimates of these values was beyond the scope of this study. We used the methodology proposed by Hardaker and Lien (2010) who advocate for the integration of frequentist and subjective distributions for variables for which data scarcity is a problem. They advise the use of distributions which are developed based on a combination of very scarce data with expert judgments. The authors argued that studies also should pay attention to issues arising when little data are available, as in the present study, because an exclusive focus on problems or questions for which either no uncertainty occurs (deterministic values would be used) or uncertainty but a large dataset is available (frequentist distributions would be used), could divert attention from more important questions, and could lead to suboptimal use of resources and investments (Hardaker and Lien, 2010). The goal of the present study was to provide recommendations to MS developers regarding which variables affect the value of their designed MS. As these results play a crucial role in guiding researchers of MS towards an optimal allocation of material, economic and human resources when optimizing their tools, the results from the sensitivity and elasticity analyses were more enriching than providing a very accurate estimate of the VoI of FAP to detect SARA. Similar to previous studies assessing the economic impact of MS (Bewley et al., 2010; Jago et al., 2011; Giordano, 2014; Down et al., 2017; Van De Gucht et al., 2018) that used simulations to investigate different situations, we examined several scenarios simulating sensitivity and elasticity analysis not only to compensate for the scarcity of data, but also to offer insights on which are the most influential factors and which combination of factors yield a positive VoI of FAP.

Our model assumed that farmers will know a priori the EMV_{all} and EMV_{none} and will choose the option entailing the highest EMV (Eq. (4)). However, this assumption may be optimistic, as farmers may lack information on the variables affecting the $EMV_{no\ monitoring}$, such as the true prevalence of SARA, the TC and the DC. Therefore, the results of the decision model presented in this study favors the decision of no monitoring over monitoring of SARA with milk biomarkers. Moreover, the results, the model, and its implications should not be extrapolated to other situations and health problems. First, the situation may be different if the MS is able to detect several health problems at once. For instance, milk FAP is also capable to predict the appearance of negative energy balance and ketosis in dairy cows (Jorjong et al., 2014, 2015). FPR is also used to assess the protein and fat percentage, important proxies for milk quality. Presumably, if the information provided by these tests also leads to improved decision making regarding other problems, their intrinsic VoI would be higher (Verstegen et al., 1995). Second, the situation would also be different if the MS changes the choice set (e.g. such as when the MS allows to change the kind of decisions that can be made). In our study, monitoring using milk biomarkers makes it possible to make decisions at the individual cow level. In contrast, when no monitoring system was used only decisions at the herd level could be made. Sometimes no herd level decision is possible, such as when using MS to detect estrus (e.g. progesterone sensor, activity meters, etc.) (van Asseldonk et al., 1999; Jago et al., 2011; Rutten et al., 2014; Giordano, 2014). The objective of this study was to investigate the economic VoI of milk biomarkers to detect SARA. Consequently, only the economic perspective was explored. However, the use of MS is considered as a means to enhance animal welfare. SARA is known to seriously impair cows' welfare as it is linked with involuntary early culling (Enemark, 2009), including the effect on animal welfare into the economic analysis may have provided higher VoI of FAP.

Furthermore, it was assumed that a representative heuristic was used by the dairy farmer when he/she faced the monitoring results used to make SARA treatment decisions. In other words, the farmer disregards the previous information about the disease and uses only the new monitoring results to treat SARA. This is a behavioral assumption that can in theory be challenged. A decision maker may react to new information in three ways: using a bayesian heuristic, a representativeness heuristic and conservativism heuristic (Tversky and Kahneman, 1982). Whether the information is embedded into a decision support system or not may have an influence on the heuristic used to make treatment decisions. For instance, if the monitoring information is accompanied by advice, the farmer may be more prone to use a representative heuristic. Previous studies reported that people rely more on simpler heuristics than the bayesian heuristic such as the representativeness and conservativism heuristics (Gans et al., 2007; Barham et al., 2014). A representativeness heuristic was hypothesized by Rutten et al. (2014) to be used by dairy farmers who might want to trust the MS blindly. In contrast, a conservativism heuristic was thought to be used by dairy farmers using estrus detection sensors because alerts generated did not result in earlier insemination nor better reproductive performance (Steeneveld et al., 2015). In the present study a sensitivity analysis of how using the three possible heuristics may affect the VoI of the MS was not performed. Further research should investigate the heuristics used by farmers when faced with the results of the MS.

5. Conclusion

The current study presents a simple stochastic decision tree model that can be used to examine the conditions under which the VoI of a MS is beneficial. Under all the simulated scenarios, decisions based on the FPR always lead to the lowest EMV. The results of our ex-ante analysis using several scenarios suggested that, on average, the VoI of FAP to detect SARA was low and did not outperform the decisions that were made without monitoring of SARA. On the contrary, when the True Prev was between 0.21 and 0.79, when the TC costs were lower than €116/case/year and DC were higher than €260/case/year, the FAP showed a positive VoI, rendering FAP an appropriate monitoring tool to identify SARA under those conditions. In addition, increasing the Sp of the test will yield a higher value than improving the Se. The results of this study can guide the developers of the FAP-based models to best allocate limited resources in their quest to design a MS to diagnose SARA. To avoid the suboptimal use of resources, we advocate that developers of MS perform an ex-ante evaluation of the potential benefits of their tools, similar to the one presented in this study, during the research phase and before they are commercialized.

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Conflict of interests

The authors disclose no conflict of interests.

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Data statement

The data used in this study can be provided upon request to the corresponding author.

Appendix A

In total four datasets were used to estimate the test characteristics of FPR (dataset 1.1, dataset 1.2, dataset 2, dataset 4) and of FAP (dataset 1.1

Table A1
Overview of the four datasets from acidosis induction experiments in dairy cows that were used to estimate the test characteristics of the fatty acid profile and fat-to-protein ratio (adapted from Colman et al., 2015).

Dataset	Number of cows	DIM[a] (μ[b] + SD[c])	Period (days)	Ration	Sampling time	Number of samples
1.1[d]	3	127 ± 61.9	33	(1) Control diet (F/C[e] ratio of 65/35) (2) Standard concentrate was replaced stepwise by wheat-based concentrate (3) Total amount of concentrate increased (4) Buffer addition (5) Control diet	Rumen pH, milk FAP[f] and FPR[g] (1st day diet 1; 4th day diet 2; 4th day diet 3; 2nd day diet 4; 4th–7th day diet 5)	49[h]
1.2[d]	3	170 ± 30.3	3 × 21	(1) Day 1 to day 13: Control diet (F/C[e] ratio of 68/32) (2) Day 14 to day 21: standard concentrate was substituted stepwise by concentrate rich in quickly fermentable carbohydrates until the total percentage of concentrate B reached 100%	Rumen pH, milk FAP[f] and FPR[g] (day 13th - day 21st of each of the 3 periods)	80[i]
2[j]	12	236 ± 42	42	(1) Week 1: control ration (2) Week 2–5: standard concentrate was gradually changed by wheat-based concentrate (3) Week 6: total concentrate is increased	Rumen pH, milk FAP[f] and FPR[g] (2nd day and 7th day of each week)	144[k]
4	3	146 ± 189	3 × 21	(1) Day 1 to day 13 starch-rich, sugar-rich or starch-and protein rich concentrate, F/C[d] ratio of 75/25 (2) Day 14 to day 18: The amount of concentrate was increased stepwise by 5% till the F/C[r] ratio reached 50/50 (3) Day 19 to day 21: the cows were fed a diet with a F/C[d] ratio of 50/50	Rumen pH, milk FAP[f] and FPR[g] (10th day and 21st day of each period)	107

[a] Days in milk.
[b] Average value.
[c] Standard deviation.
[d] Colman et al. (2012).
[e] Forage/concentrate ratio.
[f] Fatty acid profile.
[g] Fat-to-protein ratio.
[h] For one sample the ruminal pH could not be reliably measured so only 48 samples were used to estimate the sensitivity and the specificity of FAP and FPR.
[i] For two samples the ruminal pH could not be reliably measured so only 78 samples were used to estimate the sensitivity and the specificity of FAP and FPR.
[j] Colman et al. (2010).
[k] For 12 samples the ruminal pH could not be reliably measured so only 132 samples were used to estimate the sensitivity and the specificity of FAP.

and 1.2). An overview and brief description of each dataset is given below and in Table A1

Dataset 1. Colman et al. (2012) describes the experimental design, sampling and rations contained in dataset 1 which consisted of two sub-experiments (referred as to experiment 1.1 and experiment 1.2) conducted in the Netherlands (Schothorst Feed Research, Lelystad, the Netherlands). The induction of acidosis was achieved by a stepwise replacement of a standard concentrate (concentrate A) by a concentrate rich in quickly fermentable carbohydrates up to 100% (concentrate B), followed by an increase of the total amount of concentrate B. In experiment 1.1 three rumen-fistulated cows were administered five diets subsequently during 33 days. Diet 1 (control) consisted of a diet based on a forage/concentrate ratio (F/C) of 65/35. In diet 2, concentrate B replaced stepwise concentrate A until concentrate B reached 100% of the concentrate administered. In Diet 3 the total amount of concentrate B was increased depending on the cow by reaching the following F/C ratios: 48/52, 42/58, 24/76. Diet 4 consisted of a treatment with a buffer solution. Diet 5 was a control ration. A 3 × 3 Latin square design was applied in experiment 1.2 which consisted of three periods elapsing for 21 days. A control diet (F/C ratio of 68/32) was provided to three cows during the first 14 days of the period. In the last seven days concentrate B replaced stepwise concentrate A (from 100% concentrate A to 44% concentrate A and 56% concentrate B) and the amount of concentrate was increased until a F/C of 46/54. Three buffering solutions were added during the entire period.

Dataset 2. The experimental design, sampling and rations contained in this dataset are detailed elsewhere (Colman et al., 2010). The experiment lasted six weeks in total and was conducted in the Netherlands (Provimi Research and Innovation Centre, Velddriel, the Netherlands). The first week was the control week and consisted of 12 rumen-fistulated cows that were fed a mixture of grass silage and maize silage supplemented with standard concentrate according to lactation stage and milk yield. From the second to the fifth week, a wheat-based concentrate gradually replaced the standard concentrate. From the beginning, the ration was supplemented with feed additives (yeast, vitamin E and buffer) in order to prevent SARA. In the last week, depending on the cow's milk yield, the total amount of wheat-based concentrate was incremented by 2–4 kg/day.

Dataset 4. This dataset consists of unpublished data of an experiment performed in the Netherlands (Schothorst Feed Research, Lelystad, the Netherlands). In this experiment a 3 × 3 Latin square design was applied in which three dietary treatments were tested in three cows for three periods of 21 days. The three dietary treatments consisted of three concentrates, with either an average amount of fermentable crude protein and a high amount of fermentable starch (treatment 1) or sugar (treatment 2) or with a high amount of fermentable starch and a high amount of fermentable crude protein (treatment 3). During the first 13 days of the period, the cows received a diet with a F/C ratio of 75/25. From day 14 to 18 the amount of concentrate was increased in steps of 5% until the F/C ratio reached 50/50. This diet was also provided during the last three days of the 21-day period. Forage consisted of a mixture of corn silage, grass silage, and soybean meal (45/45/10).

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.livsci.2018.02.001.

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