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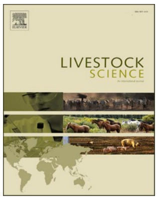

The evolutionary operation framework as a tool for herd-specific control of mastitis in dairy cows

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HIGHLIGHTS

- A "one-size-fits-all" solution does not exist for mastitis management procedures.
- We evaluated the Evolutionary Operation (EVOP) technique as a method for identifying mastitis control options in two dairy herds.
- The feasibility of the EVOP approach was demonstrated and it was appreciated by the farmers.
- The EVOP approach provided evidence for the effectiveness of different health management strategies, implemented on the studied farms.

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ABSTRACT

Mastitis is the most prevalent and costly production disease in the dairy industry, but udder health advice that helps one herd might not be beneficial for another because of "local truths". It is therefore important to identify what mastitis control options may work in a specific herd in the conditions specific to the herd. We evaluated whether the Evolutionary Operation (EVOP) methodology could be used as a management tool to identify mastitis control options to improve udder health in dairy herds. Within an EVOP framework we conducted sequences of experiments, on each of two dairy farms in Sweden. The experiments covered interventions within 1) hygiene in cubicles, 2) milking routines, and 3) dry-off procedures. Automatically recorded somatic cell counts (SCCs) in milk were used as the response variable. The impact of the interventions on SCC was evaluated with multivariate dynamic linear models. Farmer and staff satisfaction was assessed through interviews. The EVOP methodology was successfully applied, and the farmers appreciated it. We observed herd-specific variation in the effect of the interventions, indicating that EVOP would be a feasible approach to tailor mastitis control options to individual herds. Our results indicate that the EVOP methodology could be a tool to identify and evaluate health management strategies on dairy farms.

1. Introduction

Mastitis is the most prevalent and costly production disease in the dairy industry (Halasa et al., 2007). In dairy herds all over the world, there is therefore a desire to optimize udder health. Better udder health will lead to improved animal welfare, increased production efficiency, and a reduction of the use of antimicrobials. Healthy animals and a lower usage of antimicrobials will also maintain consumers' trust and support of the dairy industry.

There is an ongoing paradigm shift from the treatment of individual cows to the improved management of the whole herd, and good udder health can be achieved with preventive herd management routines. However, studies have shown that mastitis control measures are either not implemented (Nielsen and Emanuelson, 2013) or do not always

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seem to lead to permanent improvements in udder health (Emanuelson and Nielsen, 2017). Yet other studies have shown that it can be difficult to reach farmers with advice (Jansen et al., 2010, 2009). This difficulty could be partly due to the farmers' perception that the given advice is too general and not applicable to their specific herd situation. A shift from so-called "global truths" to the principles of "local truth" (Lastein, 2012) in the herd context might be the solution for better implementation and impact of management routines in individual dairy herds.

Leo Tolstoy was quoted to say, "Happy families are all alike; every unhappy family is unhappy in its own way," which is a sentiment that is now known in statistics as the Anna Karenina principle. In other words, to be happy (or healthy), a family must be simultaneously successful according to many different criteria. Failure with only one of these criteria leads to unhappiness (or poor health). Thus, there are more ways for a family to be unhappy than happy. The same idea can be applied to dairy herds. Herds with poor udder health will all have their own individual problems, but also their individual solutions (Nyman et al., 2009). Udder health advice that can help one herd might not be beneficial for another. Although there are some general principles, such as the 10-point plan of the National Mastitis Council (https://www.nmconline.org), more practical and hands-on advice needs to be tailored to each herd. One way to solve the balance between general and specific advice is to use a method called Evolutionary Operation (EVOP).

The EVOP method was originally developed in the 1950s as a manufacturing process-optimization technique (Box, 1957). The principles of the EVOP method are to introduce modifications of a manufacturing process that follow an experimental design while the manufacturing process operates at full scale and produces acceptable output. In EVOP, changes in manufacturing process variables are introduced during the normal production flow that are small enough to not adversely affect the production but significant enough to have an impact on the product characteristics. In so doing, it is possible to determine optimum process parameters and evaluate the impact of each tested parameter. Andersen et al. (2016) applied an EVOP design in a pig herd to modify the herd's normal management procedures. They concluded that the EVOP methodology can quickly provide indications of the optimal combination of production factors within a pig herd. The feasibility of the EVOP methodology has been explored as an integral part of dairy herd management (Østergaard et al., 2020; Skjølstrup et al., 2022) and has been applied on commercial dairy farms for interventions related to feeding (Stygar et al., 2017) and animal behaviour (Czubernat et al., 2020). Mastitis is a multifactorial problem and may therefore be more prone to local truths than other diseases, such that a particular intervention may or may not have the desired effect in any given herd. For this reason, the use of the EVOP method may be a reasonable approach to identify what mastitis control options may work for a specific herd in its local conditions.

The aim of this study was to determine whether the EVOP methodology could be used as a tool to identify and evaluate management options for mastitis control in specific dairy herds.

2. Materials and methods

The concept of EVOP within dairy herds relies on a few basic principles (Østergaard et al., 2020). The process should be farmer-driven and have herd-specific goals for the effect of introduced changes ("interventions") in herd management routines. The study periods for each intervention should have a short time frame and be possible to carry out without significant interference with day-to-day management of the farm. Finally, the effects of the interventions should be estimated regularly during the study period by statistical methods with frequent feedback to the farmer. In accordance with these principles, a field study was conducted on two dairy farms between August 2015 and January 2017.

2.1. Herd selection

Herds eligible for inclusion in the study had to have online somatic cell counters (OCC, DeLaval, Tumba, Sweden), because the somatic cell count (SCC) was chosen as the primary response variable in all interventions to facilitate the frequent monitoring of effects. They also should have at least two separate groups within the herd, to allow for group-wise comparisons within the herd. Finally, the herd had to have a dedicated farmer, interested in improving udder health.

To find suitable herds, herd health and livestock advisors were asked for suggestions on possible herds meeting the inclusion criteria. Several herds were identified, five farmers were contacted, and two were willing to take part in the project. Descriptions of the two herds enrolled in the project can be found in Appendix A. The herds were visited once before the start of the EVOP process to gather background information. Data collected on site was supplemented with herd specific data from the Swedish Official Milk Recording Schedule (SOMRS) database, run by Växa Sverige (Uppsala, Sweden), and other relevant information, such as results from bacteriological analyses of milk samples.

2.2. Implementation of the EVOP method

The EVOP method was implemented on the herds through a series of activities. For a more detailed description of each step in the procedure, see Østergaard et al. (2020) and Stygar et al. (2017).

1. Identification of problems and interventions. This was done at informal meetings on each farm, including the farmer, all staff members, and a veterinary advisor, with the principal investigator (the first author) present. The first step was to agree upon problem areas with potential for improvement. Then the possibilities for useful interventions in the problem areas during normal production were evaluated. Finally, the possibility of evaluating the interventions in a meaningful way was examined. As a result of these meetings, several interventions were identified for each herd (see Results and discussion section).

2. Planning of experiments based on expected intervention effect and response time. The experiments for each intervention were planned in collaboration with the farmer and the staff, and identified what should be done, by whom, and when. The experimental design, in terms of number of animals and duration, was adapted to the conditions of each herd. Forms and templates for the recording of specific information were developed in collaboration with the farmer and the staff members.

3. Intervention. All practical tasks during the experiments were done by the farmer and the staff. The herds were visited by the principal investigator three times during each intervention: at the beginning, halfway through, and at the end of each intervention. The first intervention started in September 2015 and the last intervention ended in December 2016.

4. Data collection and analysis of intervention effects. Data for evaluating the interventions was collected from the herds and the SOMRS. Somatic cell counts generated by the OCC were retrieved from the automated milking system (AMS) and calving dates were retrieved from the national cow database. Data were stored in a local database and retrieved for analysis.

The primary response variable, the SCC at each cows' milking, was averaged each day, and the natural logarithm of the daily average (logSCC) was used in the statistical analysis. A model similar to the milk yield model described by Stygar et al. (2017) was used to estimate the effect of the intervention. The two modifications to the original model were the inclusion of the effect of the AMS unit, and a reversal of the shape of the mean curve because the SCC curve had an initial decline followed by an increase, which was opposite of the curve for milk production used by Stygar et al. (2017).

Thus, if Y_{ijd} is the logSCC for cow i measured by AMS unit k on day d of lactation j, the basic model was

$$Y_{ijkd} = \mu_{jd} + \alpha_{jk} + A_{ij} + X_{ijd} + v_{ijkd} \tag{1}$$

where μ_{jd} is the average, herd specific, logSCC on lactation day d of lactation j, α_{jk} is the systematic effect of the AMS unit for lactation j, $A_{ij} \sim N(0,\ \sigma^2_{Aj})$ is a permanent lactation effect for the cow, $X_{ijd} \sim N(0,\ \sigma^2_{Xj})$ is a temporary effect of environmental factors, and $v_{ijkd} \sim N(0,\ \sigma^2_{vj})$ is a random residual. The temporary effect was modelled as a stationary first order autoregressive process with mean 0 and an autocorrelation coefficient ρ, i.e.

$$X_{ijd} = \rho_j X_{ij,d-1} + \varepsilon_{ijd} \tag{2}$$

where $\varepsilon_{ijd} \sim N(0,\ (1-\rho_j)^2\sigma^2_{Xj})$.

In this study, three logSCC profiles (for lactations 1, 2, and ≥ 3) were considered for each herd. The profiles were defined by linear functions assuming high values after calving, reaching a minimum at day δ_j and then increasing during the lactation (Emanuelson et al., 1988). Thus, we have

$$\mu_{jd} = \begin{cases} \varphi_{1j} - (\delta_j - d)\varphi_{2j},\ d \leq \delta_j \\ \varphi_{1j} - (d - \delta_j)\varphi_{3j},\ d > \delta_j \end{cases}. \tag{3}$$

All parameters were estimated in R (R Core Team, 2017) using the function lme of package nlme (Pinheiro et al., 2021) on historical data from the herds (i.e., data from 16 months before the interventions). The day [δ_j] with minimum logSCC was found as the value providing the best fit to data (measured by the log likelihood). The effect of AMS 1 was set to 0 (i.e., $\alpha_{j1} = 0$). The estimated parameters for Herd 1 and Herd 2 are shown in Appendix B, Tables B1 and B2, respectively. Graphical illustrations of the SCC profiles are shown in Fig. B1 in Appendix B.

The intervention effect on logSCC was estimated by use of a multivariate dynamic linear model (DLM). Similar to Stygar et al. (2017), observation and system equations were defined. The observation equation linked observations to the parameters, while the system equation expressed how the parameter values may change over time. However, instead of milk yield, in this study the multivariate response vector $Y_t = (y_{1t},\ \ldots,\ y_{Nt})'$ at day t consisted of observed logSCCs of all N cows that were milked on day t. A detailed description of the DLM structure is presented by Stygar et al. (2017). The DLM framework can handle several consecutive interventions as well as different study designs. It can be used to estimate an intervention effect in a study design where all cows are exposed to the change from a given day without a control group (a before-after design). It can also be used for more elaborate study designs where only a subset of the cows is exposed from a given date, and the unexposed cows thus serve as a control group. In the present study, both kinds of study design were used. In each herd, all cows and days were included in the analysis and the events were modelled as a sequence of interventions, each having a separate (additive) effect on logSCC for the cows subjected to the intervention.

In summary, the data analysis consists of the following steps: 1) The model (1) is fitted to the historical data from the herd prior to the intervention. Thus, the prior shape of the logSCC profiles is determined, and the necessary variance components for running the multivariate DLM are estimated. 2) The multivariate DLM with multivariate observation and system equations is set up exactly as described by Stygar et al. (2017). 3) The multivariate DLM is run on data from before the intervention to ensure that all parameters are calibrated to the conditions in the herd at the time of the intervention. At the time of the intervention, the intervention effect is introduced as a parameter to be dynamically estimated, and the multivariate DLM is continued. 4) The dynamically estimated intervention effect is plotted with confidence limits over time after the intervention. If the confidence limits do not include the zero line, the effect is considered as significant.

5. Evaluation. The completed interventions were evaluated in open discussions with the farmer. Decisions on continued, or future, application of treatments used in the interventions were based on the results of the intervention analysis, applicability of the new routine, and economic aspects.

2.3. *Farmers' perception*

The farmers of the study herds were interviewed to evaluate their perception of the EVOP process. The interviews were by telephone and conducted by a person that had not previously been involved in the project. The interviews were based on a prepared questionnaire and were the same for both herds. Answers on the questions were given on a scale from 1 to 10, where 1 was "Do not agree at all" and 10 "Agree completely". The questions are presented in Appendix C.

3. Results and discussion

3.1. *Identifying problems and interventions*

The process of identifying problems and interventions was similar in the two herds. All persons involved in the discussions contributed substantially to the process. The advisor, providing expertise and experience from outside the herd, had a central role in identifying problems and potential interventions. Inclusion of the staff in the process was important for both farmers, and probably contributed to their good motivation throughout the project.

Several problems, with potential effects on udder health, were readily identified in the discussions. Relevant interventions were more difficult to identify or implement. The reasons were: 1) weak (scientific) support for causal effects of identified problems and of interventions on udder health; 2) risk of interference in the running production due to extra workload or need for constructions in the barn caused by the intervention; or 3) difficulties in accomplishing a statistically sound design within the short time frame for the experiment. For these reasons, the interventions were selected on the basis of feasibility rather than on relevance.

3.2. *Identified interventions*

On each farm, a sequence of interventions were identified, including three interventions in Herd A and two interventions in Herd B. Intervention areas were hygiene in cubicles (Intervention 1, Herd A (1A)), milking routine (Intervention 2, Herd A (2A) and Intervention 1, Herd B (1B)) and dry-off routine (Intervention 3, Herd A (3A) and Intervention 2, Herd B (2B)). As two of the intervention areas were the same for the herds we report the results intervention–wise rather than experiment-wise.

Hygiene in cubicles (Herd A). The first intervention was application of a disinfectant powder (Stalosan F, Stalosan, Gråsten, Denmark) on cubicle floors, because cubicle hygiene was considered to be poor in Group 2. Due to worn out rubber mats it was difficult to clean the cubicles in Group 2 and poor cleanliness is a known risk factor for mastitis. It was decided to run an intervention where Stalosan F was used in Group 2 for 6 weeks. The powder was applied once per week, according to the manufacturer recommendations, on the floor of the cubicles in conjunction with the replacement of bedding material. All cows in the group were thus treated simultaneously and the effect within the group was analysed as a before-after design (Østergaard et al., 2020) on 135 cows.

Milking routine (Herd A and B). This intervention included a change of post-milking teat spray in the AMS. In both herds, bacteria found in the milk samples cultured from cows with clinical and subclinical mastitis 2–3 years prior to the study was a mix of contagious and environmental, both staphylococci, streptococci and coliforms. In Herd A, the teat spray with hydrogen peroxide (DeLaval Prima, DeLaval International, Tumba, Sweden) was replaced with an iodine-based spray (ProactiveTM Plus, DeLaval International, Tumba, Sweden) as intervention 2. This intervention was carried out in Group 1, the group with high SCCs, for 6 weeks and the effect was estimated on 127 cows. In Herd B, the active substance in the teat spray was lactic acid (MH-MilkAll, Agravis Raiffeisen AG, Hannover, Germany). In this herd, the spray was also replaced with an iodine-based spray (Ioklar multi, Ecolab AB, Älvsjö, Sweden). The intervention (1B) was carried out on all cows, but with a slight difference between groups in the start of the intervention in that it began 6 weeks earlier in Group 1 than in Group 2. In both herds, all cows in a group were treated simultaneously, and the effect was analysed as a before-after design.

Dry-off routine (Herd A and B). In intervention 3A and 2B, the use of a teat sealant (Boviseal, Bimeda Inc, Anglesey, Wales, UK) was evaluated. Boviseal was used routinely in Herd A at a considerable cost and the aim of the intervention was to determine whether the treatment had an effect on udder health. Teat sealant was not used in Herd B at the time of the project but had been used previously and the farmer and staff were interested in a systematic evaluation of its effect in the herd. In both herds, cows were allocated to either the treated or untreated (control) groups according to their ear number (even or uneven). The treated cows received teat sealant according to the manufacturer instructions. Cows with poor udder health, i.e., high SCCs and/or clinical mastitis in previous lactations, received the dry-off treatment with intramammary antibiotics. Teat sealant and antibiotics were applied independently. The antibiotic treatment was considered together with the intervention treatment in the analysis. In Herd A the intervention lasted 9 months with 26 treated cows and 32 control cows and in Herd B the intervention lasted 10 months with 31 treated and 34 control cows. In the analyses, the effects of 1) selective dry-off treatment with antibiotics, 2) Boviseal, and 3) both Boviseal and selective dry-off treatment with antibiotics were estimated against a control group of cows that received neither the dry-off treatment with antibiotics nor Boviseal. The effect was assessed in the beginning of the following lactation assuming a full effect on logSCC on day 5 after calving and with a linearly decreasing effect up to 42 days of milking.

3.3. Design of experiments

The design of experiments in the interventions was limited by practical conditions in the herds and the kind of intervention that was performed. In the case of cubicle hygiene (intervention 1A), group treatment was the only possible option as all cows had access to all cubicles in the group.

In the case of teat spray evaluation (interventions 2A and 1B), group treatment was also the only option because the AMS unit could only handle one teat spray at a time. An experimental design with a control group in parallel with randomly allocated treatments, which is always preferable (Østergaard et al., 2020), could have been achieved with manual milking routines. However, if manual handling increased the workload for the staff or interfered with established daily routines, as for example the addition of a disinfectant in cubicles in intervention 1A, it could be difficult to motivate the staff to run the interventions. The development of automatically administered interventions in commercial herds is therefore probably important for a successful implementation of EVOP on a broad scale in dairy farming.

The long study period of the interventions with teat sealants (interventions 3A and 2B) was far from optimal according to the guidelines (Østergaard et al., 2020). The reason for the long intervention periods was the need to get enough cows for the dry-off routine. One obvious drawback with a long study period is that farmer interest might decline during the intervention. This was not the case in this study, but it could be in another setting. Frequent reporting of results or even the possibility of the farmer and staff following the results from week to week (or day to day) might counteract this risk. A more critical aspect of the long study periods is the risk of temporal effects that might confound the results. A parallel control group design can, at least to some extent, address that concern.

3.4. Dimensioning of experiments

The dimensions of experiments were mainly determined by conditions in the herds. Power calculations were not performed to estimate the necessary number of animals to find significant differences. Instead, all available animals in a group were used for group-wise treatments, similar to a previous behavioural study (Czubernat et al., 2020). In the teat sealant interventions, the number of animals were determined by how long the intervention could be implemented. A reasonable intervention time was decided upon in discussions with the farmers and all cows that were dried off during this time were included in the experiment. These arbitrary approaches concerning sample size were far from what would be accepted in a scientific experiment, where the ability to generalize results is the aim, but might reflect the practical application of EVOP in dairy herds. An easy-to-use tool for experiment dimensioning, such as estimating necessary sample size, preferably based on the herd's own variation in the response variables, would be helpful when identifying problems and interventions. However, in herds of the size used in this study, the main problem was not the calculation of the number of animals needed, but the number of animals that were available, which might limit the chance of identifying effects. In a larger herd, interventions could be allocated to more animals and even compared between similar groups. With more animals, an intervention like the teat sealant could be conducted over a shorter time span, reducing possible effects of season and changes in herd conditions over time.

3.5. Execution of interventions

The plan was to visit the farmers regularly during the interventions to give support in running the experiment and to give feedback on intervention effects, but the visits were not frequent. However, the project management was in regular contact with the farmers by phone and email. The lack of frequent visits did not seem to be important, at least not in the short-term interventions (interventions 1A, 2A, and 1B). The farmers handled the practical issues during the experiments very well. Because the response variable was measured automatically, there was no need for extra support to make manual observations. The ability to present intervention results during the experiment would have been an advantage, especially for the long-term interventions, but a tool for a continuous evaluation was not in place when the interventions were conducted. Also, the need for regular feedback on the effects of the intervention is questionable. One argument for regular feedback is that the farmer should be able to decide whether to continue or discontinue the intervention when a significant effect can be seen, which is at the heart of the EVOP approach (Østergaard et al., 2020). However, the farmers in this study were more interested in whether or not the intervention effect was consistent than in getting frequent feedback on the general study progress.

3.6. Effects of interventions

We saw a positive intervention effect on SCC after application of the disinfectant powder on the cubicle floors (Fig. 1). There is a well-known association between clean cows and good udder health (Schreiner and Ruegg, 2003), and the disinfectant used in intervention 1A in our study has proven effective at least in experimental studies (Wattanaphansak et al., 2009).

We also saw a positive intervention effect on SCC after the introduction of a post-milking teat dip with iodine, but only in Herd A, while no effect could be seen for Herd B (Fig. 2). In earlier studies, the effect of different active ingredients in teat dips/sprays have been shown to differ between pathogens (Enger et al., 2014; Fitzpatrick et al., 2019, 2022). In both herds, it was difficult to see a pattern in the mastitis causing bacteria and depending on the most abundant bacteria at the time of the experiment, the outcome might have differed according to the

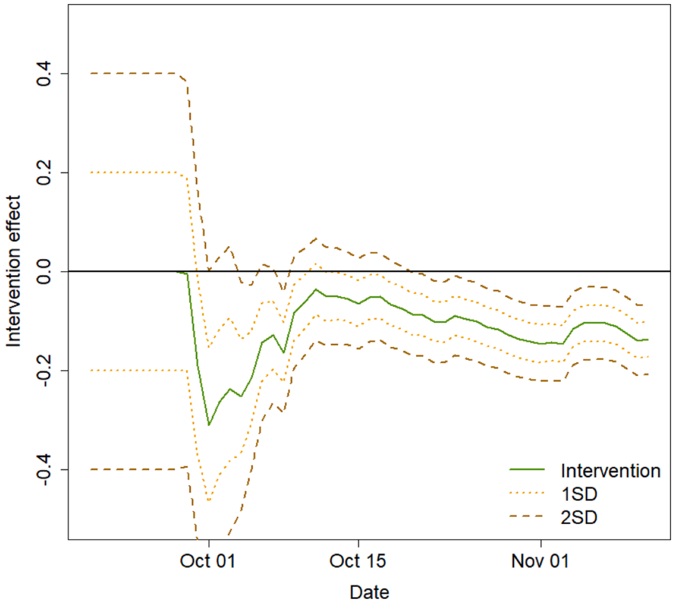

Fig. 1. Estimated average effect for Herd A of applying a disinfectant powder in cubicles to improve hygiene (Intervention 1) on log somatic cell counts, together with confidence intervals based on standard deviation (SD). If the confidence limits do not include the zero line, the effect is considered as significant.

pathogen's sensitivity to the teat disinfection product. Fitzpatrick et al. (2021) suggests that "when choosing a teat disinfectant product, the bacteria in the dairy herds' environment should be considered", which might be difficult in herds with a very heterogeneous bacterial panorama. In these herds, one can try to change teat dip/spray from one substance group to another and evaluate the change carefully.

Neither of the treatments at dry-off in intervention 3A had an observable effect on the SCC (Fig. 3), although the application of internal teat sealants at dry-off has previously been shown to significantly reduce the incidence of intramammary infections and clinical mastitis in lactating dairy cows (Rabiee and Lean, 2013).

The intervention effects differed between herds and the outcome was not always as expected according to the literature. As a result, advice needed to be tailored for each herd, which pointed to the usefulness of "experiments" with a close follow-up of effects, such as the EVOP approach. It was, however, important to consider the effect of the study design when evaluating the results. Although the herds were large by Swedish standards, it would have been preferable to have a larger number of cows available for evaluating the different interventions. The intervention of the dry-off routine was conducted over a large time frame, which might have affected the result, as conditions vary with season, and probably made the analysis less accurate.

3.7. *Evaluation of interventions*

The evaluation of interventions included the effects of the experiments on the SCC, but also the practical aspects of applying the treatments and their cost. The results of the interventions and the plan going forward was discussed on each farm with the principal investigator, the farmer, and the staff. The advisors were not involved in these meetings, which probably had a negative effect on the EVOP implementation. Draper and Box (1970) suggested an EVOP committee, composed of personnel at the production unit and specialists with different backgrounds, to assist the industrial manager in interpreting the results of the EVOP programme and deciding upon the actions to be taken for improved operations. In a dairy herd, such a committee could include the herd veterinarian as well as the production advisor in addition to the farm owner and staff when the focus was to implement the EVOP approach for a specific subject area, such as udder health. If interventions were to be implemented on a broader level on a farm, the committee could be the herd advisory board, consisting of a production advisor, economy consultant or bank representative and another farmer, which several dairy producers have connected to their business, in addition to the farm owner and a staff representative. An important role for an EVOP committee would be to help leverage any new ideas for improvement that may arise when implementing the EVOP procedure. In so doing, the EVOP process would serve as a means for both generating and evaluating suggestions for improving herd performance.

The decision to continue with an intervention, after the trial period, was usually made based on a balance of several aspects. For example, intervention 1A, the application of a disinfectant on cubicle floors, was not adopted by the farmer, despite a positive effect, as it was considered too labour intensive to fit in the running production. However, the new teat spray tested on Herd A (intervention 2A) was kept as a permanent

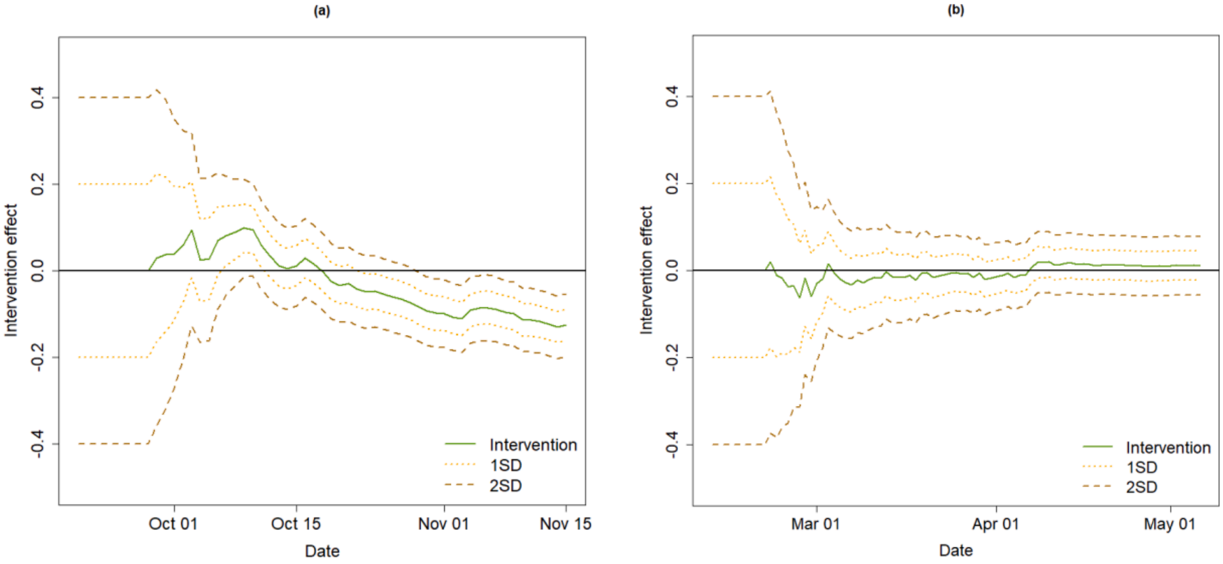

Fig. 2. Estimated average effect of milking routine, change of post-milking teat spray in the automated milking system (Intervention 2, Herd A and Intervention 1, Herd B), on log somatic cell counts, together with confidence intervals based on standard deviation (SD) for Herd A (a) and Herd B (b). If the confidence limits do not include the zero line, the effect is considered as significant.

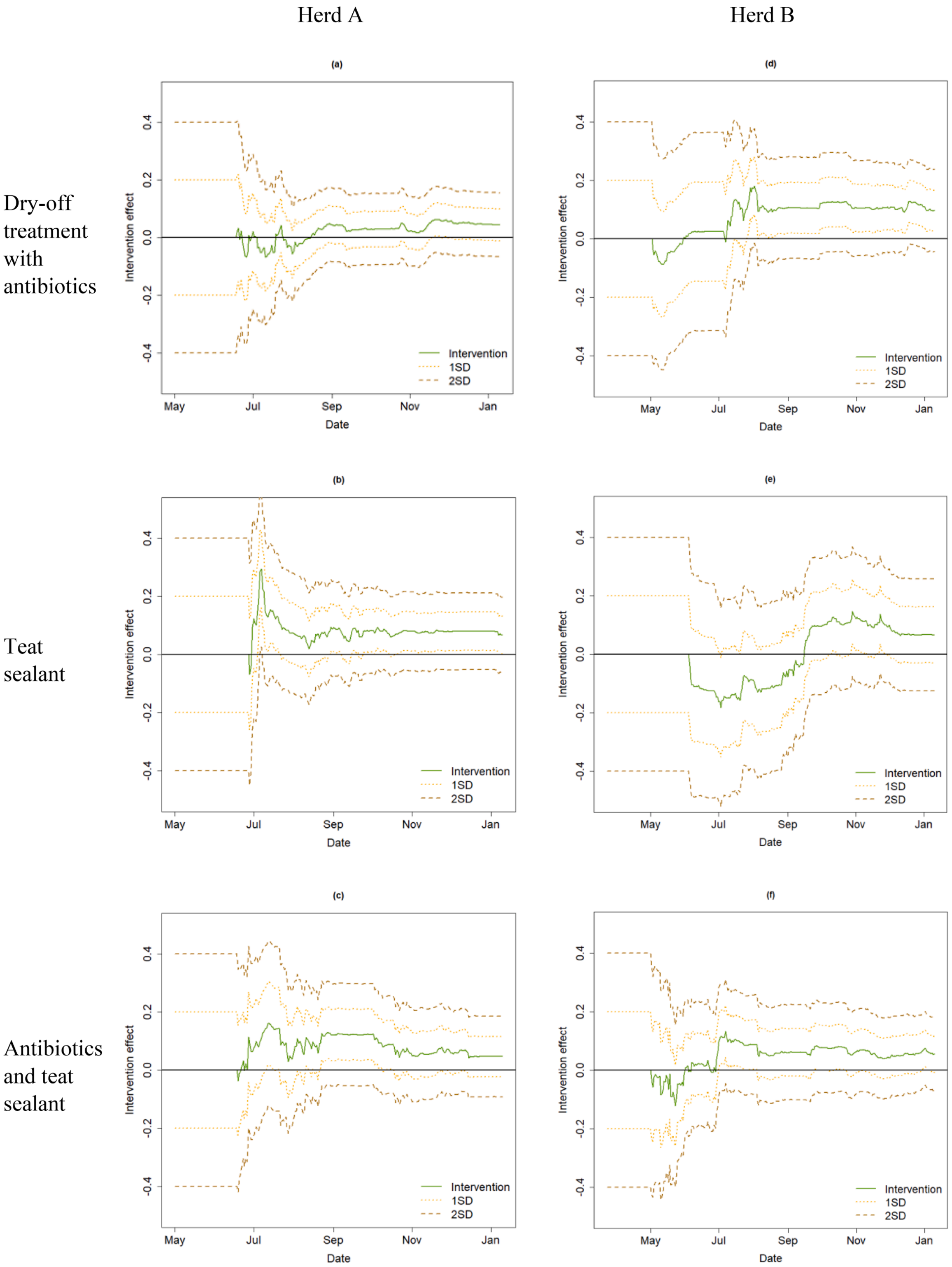

Fig. 3. Estimated average effect of dry-off routine (Intervention 3, Herd A (a, b, c) and Intervention 2, Herd B (d, e, f)) on average log somatic cell counts at the beginning of the following lactation, together with confidence intervals based on standard deviation (SD). If the confidence limits do not include the zero line, the effect is considered as significant.

routine, which was supported by the intervention results. In Herd B, we did not find a detectable effect of the new teat spray, but the new routine was maintained. The decisions to keep the teat spray in both herds was probably influenced by the lack of extra work or additional costs associated with the new routine.

A difficulty in evaluating the interventions was to determine when an effect was good enough. Even an effect that was not statistically significant could be relevant at the farm level, and vice versa. One solution would be to decide a response level at which the intervention should be considered desirable, which could be an only marginally positive effect if the cost of implementing the intervention is nil or very low (Andersen et al., 2016).

3.8. Farmers' perceptions

The farmers of both herds had positive perceptions of the EVOP concept and gave it 10 points on a 10-point graded scale, where 10 was positive and 1 was negative. They could see themselves using this concept in the future, which is consistent with the findings of Østergaard et al. (2020). One of the farmers appreciated the systematic testing of one new management routine at a time. The staff of both herds were highly motivated to conduct the interventions: motivation scored 8 in Herd A and 10 in Herd B. Not all staff members in Herd A appreciated the changed routines, which probably influenced the score negatively. The interventions that were more or less automatically applied with automatic treatments, such as comparing teat sprays, were considered very easy (10 points) to conduct. Applying the disinfectant on cubicle floors in Herd A scored 7, probably due to the extra workload. The teat sealant intervention scored 4 in Herd B, probably because the extra work was a bit demanding. Both farmers thought that the EVOP process could be integrated in an advisory service. To limit expenditures, the EVOP process could, for example, be a part of one of the existing service packages for improving herd health that is offered by advisory companies.

3.9. EVOP as a tool for improving animal health in dairy herds

The idea from Box (1957) that an optimum in a process can be found by stepwise adjustment and evaluation of process variable levels is useful under many conditions, but a farm is not a factory and the idea may not be as easy to apply. It could have been applied in Intervention 1 in Herd 1, in which the disinfectant powder could have been administered at intervals other than weekly in a subsequent intervention, such as every second week or twice per week. This was not considered, because the negative attitude among the staff towards the routine meant it was terminated after the trial period. The other interventions were not suitable for stepwise adjustments because they were binary in nature (i.e., either used or not used), which is probably often the case in dairy production. In a typical industry setting such as a factory, conditions can be maintained at a relatively constant level over time, meaning that one step towards an optimum can give a new starting point for the next step. Pig and poultry production, with batch-wise rearing of animals that are more genetically homogenous, is more similar to industrial production than dairy production and may therefore be more suitable for experiments according to the original EVOP concept.

In the original application of the EVOP concept (Box, 1957), the response variable was a direct measure of the outcome and the input variables, or treatments, were factors known to have direct effects on the outcome. This is different from the application of EVOP in this project where the response variable, SCC, is an indirect measure of the outcome, udder health. Andersen et al. (2016) also used an indirect response, drinking patterns in pigs, as an indicator of stress, because the large variation in the economically interesting response, live weight gain, would mask an eventual response. When the EVOP concept is used to improve health in dairy herds, indirect response variables are preferable because incidences of disease often are too rare to be useful as response variables if intervention periods need to be kept reasonably short. The continuous development of new sensor techniques to measure animal response in general at the herd level would therefore be helpful for the application of the EVOP method. These measurements are also automatically recorded to limit extra work, which is another prerequisite. Several sensor systems have been developed and are commercially available for the detection of mastitis, locomotion problems, fertility, metabolic disorders, and welfare in dairy cows (Rutten et al., 2013; Stygar et al., 2021), thus improving the possibility of applying the EVOP method in dairy herds to improve animal health and welfare.

An advantage of a more frequent use of the EVOP methodology could be to provide more evidence for the effectiveness in practice of the variety of health management strategies that are suggested and applied based on research. It would also increase the trust of farmers because the outcome has been achieved with the active involvement of their peers.

4. Conclusions

It was feasible to apply the EVOP methodology to mastitis management in the two dairy herds, and the farmers appreciated the approach. However, its usefulness may be constrained by farm-specific conditions, making its application less than optimal in some cases. Farm-specific effects of interventions on udder health were found, which suggest that local experimentation, and thus an EVOP approach, would be useful to find appropriate mastitis management for individual dairy herds.

Author agreement statement

We the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We understand that the Corresponding Author is the sole contact for the Editorial process. He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A

Description of the two herds

Herd A was located 340 km north of Uppsala. Two employees, together with the farmer, managed 140 Swedish Holstein cows housed in a free stall barn during the lactating period and on deep straw bedding during the dry period. Cows were milked in two automatic milking system (AMS) units (VMS, DeLaval, Tumba Sweden), AMS 1 and AMS 2, equipped with online somatic cell counters (OCCs, DeLaval, Tumba, Sweden). The cows were kept in two groups: Group 1 (milked in AMS 1), which included primarily older cows, and Group 2 (milked in AMS 2), which included mainly primiparous and young cows. The herd produced on average 12,000 kg of milk per cow per year and the average bulk milk SCC was ~240,000 cells/mL. Approximately 25 % of the cows were treated for clinical mastitis on a yearly basis, which is above the Swedish average. After weaning, heifers were reared and inseminated by a contractor. They returned to the herd shortly before calving.

Herd B was located 50 km north of Uppsala. Two employees and the farmer handled a herd of 150 Swedish Red and Swedish Holstein cows. Like Herd 1, cows were housed in free stalls during the lactating period and milked in two AMS units (VMS, Delaval, Tumba, Sweden) equipped with an OCC (DeLaval, Tumba, Sweden). Similar to Herd A, the cows in Herd B were kept in two separate groups: Group 1 (AMS 1), with a majority of older cows, and Group 2 (AMS 2), with mainly primiparous and younger cows. The herd produced on average 11,000 kg milk per cow per year and average bulk milk SCC was 260,000 cells/mL. About 5 % of the cows were treated for clinical mastitis. Dry cows and heifers were housed on deep straw bedding.

Appendix B

Table B1
Estimated parameters for the log somatic cell count (logSCC) model for Herd A[1].

Parameter	Symbol[2]	Lactation 1	Lactation 2	Lactation ≥ 3
Day with minimum logSCC	δ_j	30	25	15
LogSCC at minimum	φ_{1j}	4.62 (0.12)	4.53 (0.09)	4.80 (0.08)
Slope before minimum	φ_{2j}	-3.84×10^{-2} (0.003)	-2.02×10^{-1} (0.004)	-3.10×10^{-2} (0.005)
Slope after minimum	φ_{3j}	-1.15×10^{-3} (0.0002)	-1.89×10^{-3} (0.0003)	-2.12×10^{-3} (0.0003)
Effect of automatic milking system 2	α_{j2}	-8.05×10^{-1} (0.103)	-3.37×10^{-1} (0.061)	-5.18×10^{-1} (0.100)
Variance of lactation effect between cows	σ^2_{Aj}	0.220	0.239	0.328
Variance of temporary effect	σ^2_{Xj}	0.289	0.308	0.466
Residual variance	$\sigma^2_{\nu j}$	0.240	0.283	0.294
Auto-correlation of temporary effect	ρ_j	0.850	0.901	0.982

[1] standard deviation in parentheses.
[2] *j* in the subscript refers to lactation number.

Table B2
Estimated parameters for the log somatic cell count (logSCC) model for Herd B[1].

Parameter	Symbol[2]	Lactation 1	Lactation 2	Lactation ≥ 3
Day with minimum logSCC	δ_j	30	15	10
LogSCC at minimum	φ_{1j}	3.82 (0.01)	4.21 (0.08)	5.09 (0.08)
Slope before minimum	φ_{2j}	-4.08×10^{-2} (0.003)	-7.02×10^{-2} (0.007)	-6.68×10^{-2} (0.014)
Slope after minimum	φ_{3j}	-2.36×10^{-3} (0.0003)	-1.78×10^{-3} (0.0003)	-2.44×10^{-4} (0.0004)
Effect of automatic milking system 2	α_{j2}	7.63×10^{-3} (0.0865)	4.05×10^{-2} (0.0662)	3.70×10^{-1} (0.0491)
Variance of lactation effect between cows	σ^2_{Aj}	0.267	0.299	0.333
Variance of temporary effect	σ^2_{Xj}	0.255	0.345	0.435
Residual variance	$\sigma^2_{\nu j}$	0.435	0.502	0.432
Auto-correlation of temporary effect	ρ_j	0.970	0.964	0.984

[1] standard deviation in parentheses.
[2] *j* in the subscript refers to lactation number.

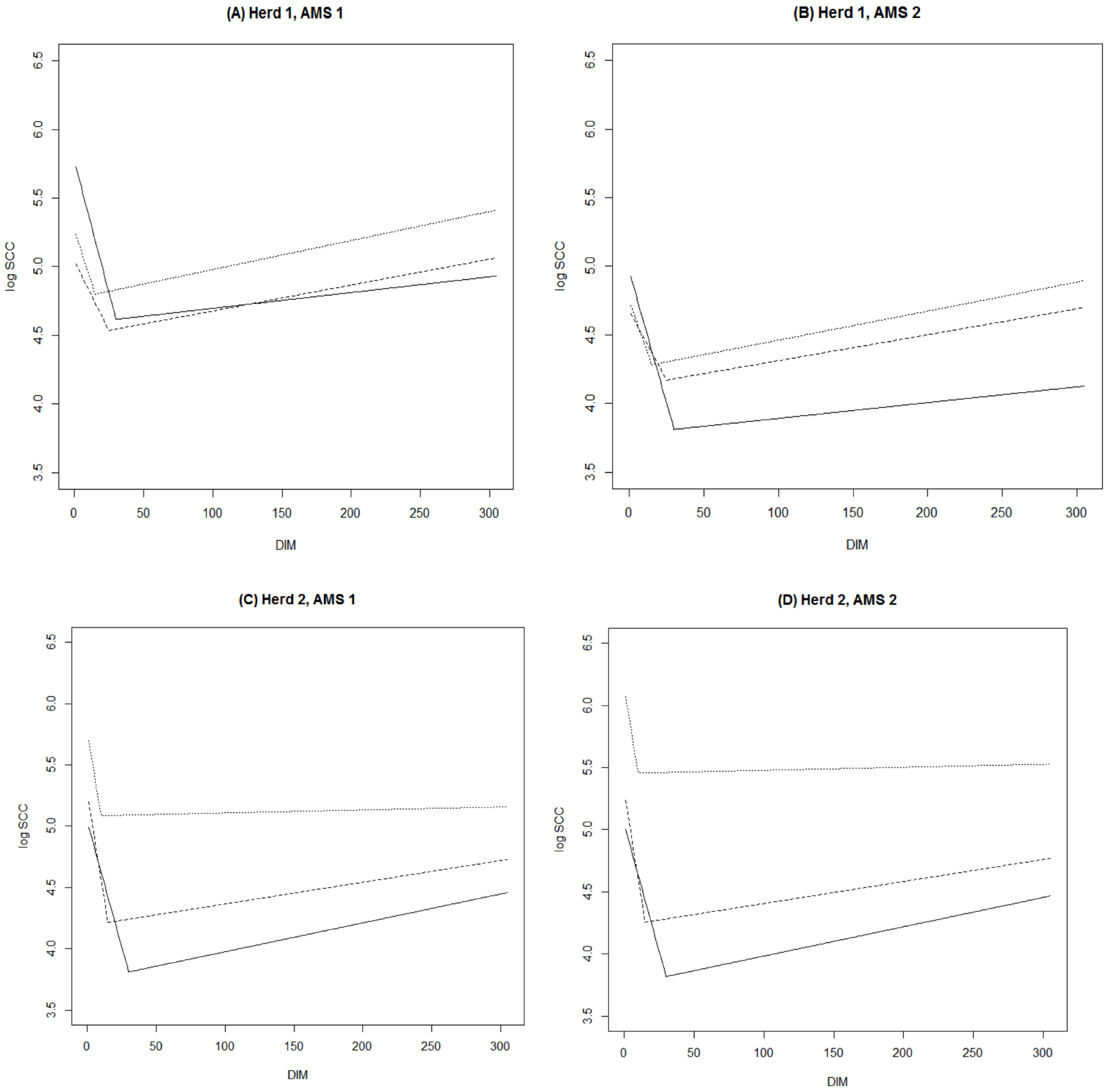

Fig. B1. Cell count profiles (mean log somatic cell count (logSCC) as a function of days in milk (DIM)) for parities 1 (solid line), 2 (dashed line), and ≥ 3 (dotted line) estimated based on available historical data for (A) Herd A, automatic milking system (AMS) 1, (B) Herd A, AMS 2, (C) Herd B, AMS 1, and (D) Herd B, AMS 2.

Appendix C

Questions used when interviewing the farmers.

1. Who came up with the idea for the interventions you tried?
2. How difficult was it to carry out the interventions (grade on a scale from 1 to 10, where 1 is very difficult and 10 is very easy)? If there were multiple interventions, state for each.
3. What problems arose during implementation?
4. To what extent was everyone who works with the dairy cows involved in the project, i.e. willing to implement the interventions (grade on a scale from 1 to 10, where 1 is not at all and 10 is completely)?
5. Have you come up with ideas for other interventions to evaluate with the EVOP concept (yes/no)?
6. If so, which ones?
7. Are there things in the project that could have been done differently, from a retrospective point of view?
8. What do you think about the EVOP concept itself, i.e. to systematically test interventions in the herd and carefully follow up and evaluate the result (grade on a scale from 1 to 10, where 1 is very negative and 10 is very positive)?
9. Would you consider working in line with the EVOP concept in the future, i.e. to systematically evaluate changes in routines and management of the dairy cows (grade on a scale from 1 to 10, where 1 is not at all likely and 10 is very likely)?
10. Do you think that such a systematic evaluation could be integrated into the advisory services you use (yes/no)?
11. If so, how?

12. Any other comments?

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