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Monitoring the udder health in dairy herds

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ALLEN, DIE ES SCHON IMMER GEWUSST HABEN

TABLE OF CONTENTS

I. INTRODUCTION

The infectious inflammation of the udder gland is one of the most common diseases of dairy cows and causes substantive costs (Petrovski et al., 2012). Frequent mastitis not only compromises the economic situation of a dairy herd but also reduces the satisfaction of the farmer with his work (Jansen et al., 2009) and affects animal welfare (Leslie and Petersson-Wolfe, 2012). The monitoring, that is the routine collection and analysis of information about the occurrence of mastitis and the evaluation of management practices, is a substantial part of the management of the udder health on dairy farms (Lam et al., 2011). In this thesis recommendations for different aspects of the monitoring of the udder health on dairy farms shall be given.

The implementation of the „5-point-plan“ (regular maintenance of the milking machine, teat disinfection after milking, treatment of clinical mastitis, antibiotic treatment at drying-off and culling of chronically infected cows) reduced the number of intramammary infections caused by cow-associated mastitis pathogens like *Staphylococcus aureus* and *Streptococus agalactiae* in regions with intensive dairy farming (Barkema et al., 2009; Ruegg, 2012). Therefore, intramammary infections gained in importance, that are caused by pathogens whose reservoir is the environment of the cow. Usually, they are not considered to be contagious and are called “environmental pathogens”. Environmental mastitis is a multifactorial disease and it is considerably more complex to prevent (Krömker and Friedrich, 2009; Ruegg, 2012; Schukken et al., 1989; Smith, 1983). Consequently, the recommended udder health programs were intensively specified, now covering not only the milking and the mastitis therapy but nearly the whole life of a dairy cow (genetics, housing, management, nutrition, milking, health status of the herd) (Krömker and Friedrich, 2009; National Mastitis Council (NMC), 2006). Udder health programs became so all-encompassing that fulfilling every point of the lists on a farm without prior cost-benefit-analysis may lead to considerably increased expenditures without appropriately reducing the losses (Morin et al., 1993). The monitoring is a part of the current udder health programs (National Mastitis Council (NMC), 2006).

The National Mastitis Council (NMC) defines the monitoring as “the routine systematic collection and evaluation of information from the farm, intended to identify problem areas, and to track performance over time” (National Mastitis Council

(NMC), 2002). On a dairy farm, the monitoring provides quantitative information as a foundation for decisions and allows to control production and animal health. It can be applied to different levels of production depending on its purpose:

- to the product level (e.g., the amount and quality of delivered milk) to assess the economic performance of the herd,
- to the animal or disease level (e.g., the percentage of cows with mastitis or number of mastitis cases per year) to keep track of the disease status of the herd and,
- to the risk factor level for mastitis (e.g., the percentage of cows with impaired teat condition) to keep the risk of mastitis for the herd under control.

The latter two levels may be combined as the process level. The monitoring at the process level is recommended for improving and sustaining a good udder health on a herd level (Krömker, 2007; Schukken et al., 2003; Winter, 2009) and is one of the ten points of the „NMC recommended mastitis control program“ (National Mastitis Council (NMC), 2006). Jansen et al. (2009) found correlations between conducting monitoring activities (e.g., checking individual cows' cell count or the bacteriological investigation of clinical mastitis cases) and the improvement of the udder health of dairy herds.

The overall objective of the present cumulative thesis was to develop science-based recommendations for different aspects of the monitoring of the udder health on dairy farms on the product level as well as on the process level. On the process level, variables for monitoring the teat condition and metabolic disorders as possible risk factors for mastitis should be investigated. On the product level, a method to assess milk yield loss due to clinical mastitis in individual dairy herds should be developed. The results of the separate studies should be published in peer-review scientific journals.

A practical approach to monitor the udder health was described in a literature review because monitoring all possible risk factors for mastitis on a dairy farm is neither realistic nor economically sensible. Therefore, it is necessary to identify by risk analysis the essential variables for a particular farm and time that have to be monitored in order to control the most relevant risk factors (Krömker and Friedrich, 2011; Reneau and Kinsel, 1998). Subsequently, the expenditures for each monitoring measure have to be compared to the expected value of the information gained at that point. All diagnostic measures are useless as long as deviant results do not lead to actions different to those which would be taken without them (Mansfeld et al., 2007; Natzke, 1981). The review has been published in Tierärztliche Praxis G (Impact factor 2014: 0.470):

> ZOCHE, V., HEUWIESER, W., KRÖMKER, V., 2011. Risikoorientiertes Monitoring der Eutergesundheit - Eine Literaturübersicht. Tierarztl Prax Ausg G Grosstiere Nutztiere 39, 88–94.

The monitoring is an essential part of mastitis control programs to achieve and maintain a good udder health on dairy farms in the long term. It is necessary for:

- routine evaluations of the herd health and performance status (Kelton, 2006; Krömker, 2007; Reneau and Kinsel, 1998; Schukken et al., 2003),
- the continuous verification of the effectiveness of actions taken to improve the herd status (Green et al., 2010; Krömker, 2007; Reneau and Kinsel, 1998) and,
- the early identification of emerging problems (Reneau and Kinsel, 1998; Winter, 2009). Ideally, variables are monitored that additionally provide information on possible causes of the problems (Noordhuizen and Welpelo, 1996; Reneau and Kinsel, 1998).

For these purposes, key indicators describing the udder health and the risk factors for mastitis should be monitored (Krömker, 2007; Schukken et al., 2003). Dohoo (1993) pointed out that it was the task of veterinary epidemiology to provide evidence about risk factors for production diseases and to recommend variables to monitor them. In the present thesis, the associations between variables that can be used to measure risk factors for mastitis from two different areas (the milking and the metabolic health) were investigated in two own field studies.

Machine-milking induced alterations of the teat tissue can be used to evaluate the milking process (Hamann, 1997). They may impair local defense mechanisms, and increase the risk of new intramammary infections (O'Shea, 1987). Mein et al. (2001) presented a simple classification scheme to quantify the proportion of cows with an

impaired teat condition and to assess the risk of new intramammary infections. The influence of the teat condition on the risk of naturally occurring new intramammary infections, inflammatory responses and mastitis was investigated in a longitudinal study. The teat condition was evaluated according to Mein et al. (2001). The paper reporting the results of the study has been published in the Journal of Dairy Science (Impact factor 2014: 2.550):

> ZOCHE-GOLOB, V., HAVERKAMP, H., PADUCH, J.-H., KLOCKE, D., ZINKE, C., HOEDEMAKER, M., HEUWIESER, W., KRÖMKER, V., 2015. Longitudinal study of the effects of teat condition on the risk of new intramammary infections in dairy cows. J. Dairy Sci. 98, 910–917.

The objective of the second field study was to evaluate the association between the milk fat-protein ratio and the occurrence of clinical mastitis. Milk fat and protein percentages are determined monthly in the regular tests of the dairy herd improvement association and their ratio is recommended to monitor the energy balance of dairy cows (Buttchereit et al., 2010; Heuer et al., 1999; Krogh et al., 2011). A severe negative energy balance impairs the immune system and consequently may increase the risk of clinical mastitis (Goff, 2006). The article describing this study is in press at Preventive Veterinary Medicine (Impact factor 2014: 2.506) on February 24, 2015:

> ZOCHE-GOLOB, V., HEUWIESER, W., KRÖMKER, V. Investigation of the association between the test day milk fat-protein ratio and clinical mastitis using a Poisson regression approach for analysis of time-to-event data. PREVET (2015). http;//dx.doi.org/10.1016/j.prevetmed.2015.06.018.

For a dairy farmer, it is important to know the monetary loss due to mastitis on his specific farm, so that he can decide about investments in control measures. Losses due to mastitis are mainly determined by the reduction in milk yield (Hogeveen et al., 2011; Petrovski et al., 2012; Seegers et al., 2003). The reduction of milk yield caused by mastitis differs significantly between farms (Huijps, 2009; Seegers et al., 2003). Therefore, herd-specific estimations are needed as a basis for management decisions. As part of the computer program “Daten- und Informationsplattform Tier (DIT)” of the Saxon dairy herd improvement association (Sächsischer Landeskontrollverband e. V.), a model was developed to estimate the milk loss caused by clinical mastitis for a specific dairy herd based on individual cow’s mastitis and daily milk yield data. The model was presented in a paper published in Berliner und Münchener Tierärztliche Wochenschrift (Impact factor 2014: 0.931):

> ZOCHE-GOLOB, V., SPILKE, J., 2013. Herdenspezifische Schätzung der Milchleistungsminderung durch wiederholte klinische Mastitis. Berl. Munch. Tierarztl. Wochenschr. 126, 269–276.

The integration of the developed model in the computer program would allow to monitor the milk yield losses due to clinical mastitis. Using herd-specific estimates of milk yield losses, decisions about investments in preventive measures can be made on a better foundation. Additionally, the comparison to the herds with the least losses allows to assess the possible profit of a dairy farm for improving udder health (Zoche-Golob and Spilke, 2013).

II. REVIEW ARTICLE

Risikoorientiertes Monitoring der Eutergesundheit – Eine Literaturübersicht

This article has been published in Tierärztliche Praxis G (Impact factor 2014: 0.470):

ZOCHE, V., HEUWIESER, W., KRÖMKER, V., 2011. Risikoorientiertes Monitoring der Eutergesundheit - Eine Literaturübersicht. Tierarztl Prax Ausg G Grosstiere Nutztiere 39, 88–94.

http://www.schattauer.de/t3page/1214.html?manuscript=16040

III. RESEARCH ARTICLES

Longitudinal study of the effects of teat condition on the risk of new intramammary infections in dairy cows

This article has been published in the Journal of Dairy Science (Impact factor 2014: 2.550):

ZOCHE-GOLOB, V., HAVERKAMP, H., PADUCH, J.-H., KLOCKE, D., ZINKE, C., HOEDEMAKER, M., HEUWIESER, W., KRÖMKER, V., 2015. Longitudinal study of the effects of teat condition on the risk of new intramammary infections in dairy cows. J. Dairy Sci. 98, 910–917.

http://dx.doi.org/10.3168/jds.2014-8446

Investigation of the association between the test day milk fat-protein ratio and clinical mastitis using a Poisson regression approach for analysis of time-to-event data

This article is in press at Preventive Veterinary Medicine (Impact factor 2014: 2.506):

ZOCHE-GOLOB, V., HEUWIESER, W., KRÖMKER, V. Investigation of the association between the test day milk fat-protein ratio and clinical mastitis using a Poisson regression approach for analysis of time-to-event data. PREVET (2015).

http://dx.doi.org/10.1016/j.prevetmed.2015.06.018

Herdenspezifische Schätzung der Milchleistungsminderung durch wiederholte klinische Mastitis

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ZOCHE-GOLOB, V., SPILKE, J., 2013. Herdenspezifische Schätzung der Milchleistungsminderung durch wiederholte klinische Mastitis. Berl. Munch. Tierarztl. Wochenschr. 126, 269–276.

http://dx.doi.org/10.2376/0005-9366-126-269

IV. DISCUSSION

As herd sizes increase, the continuous monitoring becomes more important for dairy farmers and their consultants to maintain udder health. To avoid unnecessary expenditures for monitoring measures, recommendations are needed how to set up a monitoring system for a farm and which indicators could be helpful. Tools that simplify data analysis for monitoring purposes have to be developed.

In a literature review, a risk-based approach for monitoring udder health was presented. This approach is a workable alternative to the monitoring of all conceivable factors as postulated in the guidelines for the implementation of veterinary herd care on dairy farms of the Federal Association of Veterinary Practitioners (Bundesverband praktizierender Tierärzte e. V. (bpt), 2011), and to the monitoring of the mastitis level only without the risk factors. The major advantages of risk-based monitoring were that the efforts would be focused on the relevant risk factors for mastitis on a specific farm without completely loosing track of the other factors. Thus, the cost-benefit-ratio for the monitoring of the udder health could be optimized.

There are too many variables which can be used to monitor the udder health on the process and the product levels to be treated in a single given study. Recommendations about variables that could be used to monitor the mastitis level of a dairy herd were available from several publications (e.g., Schukken et al., 2003). For this reason, I chose to focus on the monitoring of the risk factors for mastitis and on the monitoring of the economic effects of mastitis. Variables that can be used to monitor the teat condition and metabolic disorders as possible risk factors for mastitis were investigated. A model was developed which can be used to assess the milk loss due to clinical mastitis for a specific dairy herd.

To my knowledge, this is the first field study evaluating associations between short-term as well as long-term changes in the teat condition and the risk of naturally occurring new intramammary infections with different pathogens and new inflammatory responses. No variable of short- or long-term changes in the teat condition was associated with a changed risk of an udder quarter for any kind of new intramammary infection, new inflammatory responses, or new mastitis. A longitudinal design was chosen because causal inference is only possible, if the time series of events can be

clearly defined (Reyher et al., 2013). However, longitudinal studies with repeated determination of the teat condition and the infectious status are time consuming (Zadoks et al., 2001); a fact that limited the number of animals which could be included in the study. The number of observations available for the statistical analysis was further reduced because only two udder quarters per cow could be investigated. Additionally, only few new intramammary infections caused by environmental pathogens (coliform bacteria and streptococci other than *Strep. agalactiae* and *Strep. dysgalactiae*) were observed. Probably, most infections with environmental pathogens were missed because the sampling interval was one month and the geometric means of the duration of intramammary infections with coliforms and environmental streptococci were 9 and 17 days, respectively (Smith et al., 1985). Consequently, if the teat condition influences the risk of new intramammary infections or new inflammatory responses only slightly, these associations could not be found in the study. Until now, any effects of short-term changes in the teat condition on new intramammary infections or new inflammatory responses have not been proven. There were only few studies that suggest an effect of teat end hyperkeratosis on the udder health (Breen et al., 2009; Dingwell et al., 2004; Neijenhuis et al., 2001; Zadoks et al., 2001). Particularly, extreme teat end hyperkeratosis seemed to increase the risk of clinical mastitis (Breen et al., 2009; Neijenhuis et al., 2001).

The data of the first study suggested that if the teat condition does influence the udder health, the impact will be small. Neither short- nor long-term changes in the teat condition could be considered as risk factors for mastitis and monitoring them would be wasted effort in most cases. Further research is warranted to determine if there are certain circumstances or pathogens, when the teat condition becomes more important for the udder health.

In the second study, significant associations between the test day milk fat-protein ratio and the occurrence of clinical mastitis were found. Fat-protein ratios below 1.0 and above 1.5 were both associated with higher clinical mastitis incidence rates compared to a fat-protein ratio between 1.0 and 1.5, but their respective influence was small. The influence of a fat-protein ratio >1.5 increased over the course of the lactation period. This was interesting because severe negative energy balance (indicated by fat-protein ratios >1.5) is commonly seen as a postpartum disorder in dairy cows (Fleming, 2002) and is rare after 100 days in milk. But any disease that decreases feed intake may cause secondary ketosis (Fleming, 2002) and consequently lead to an increased fat-protein ratio. Probably, both (the impaired health condition, and as consequence the

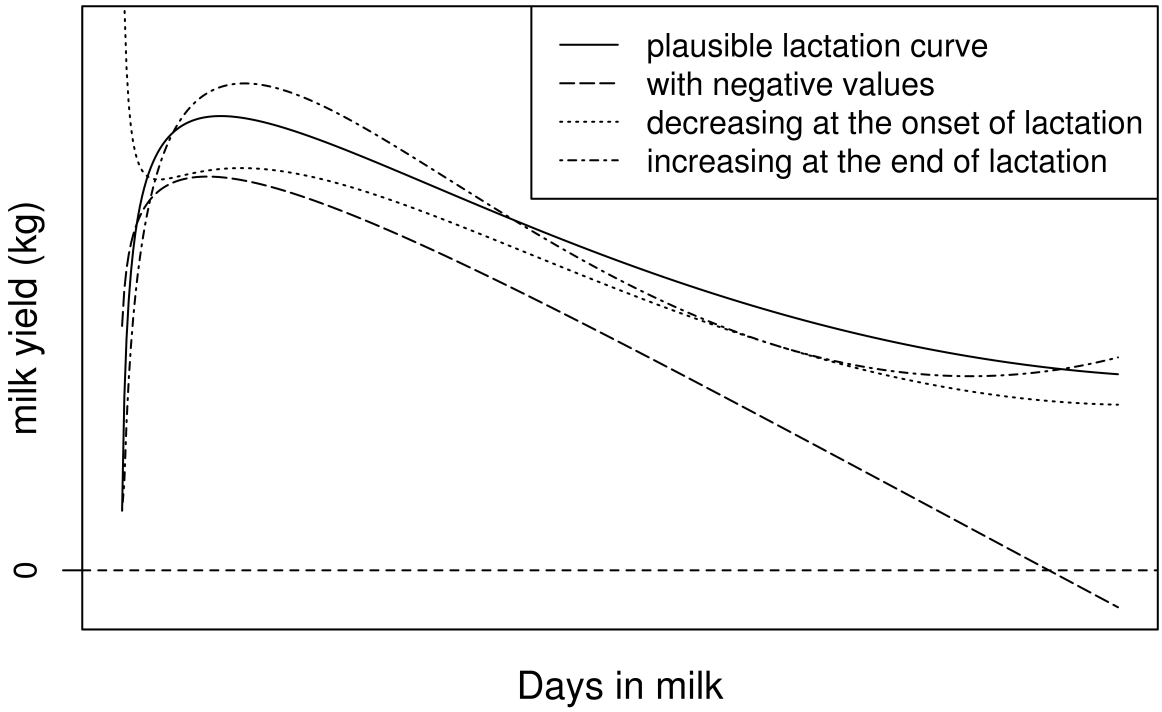
severe negative energy balance of cows after 100 days in milk) increase the susceptibility to clinical mastitis. As conclusion of this study, the usage of the fat-protein ratio to monitor metabolic disorders as risk factors for clinical mastitis could not be recommended because its ability to predict clinical mastitis seemed to be low. Therefore, other measures to monitor metabolic disorders as risk factors for mastitis like e.g. cow-side tests for (subclinical) ketosis should be evaluated.

A mixed Poisson regression model with the weekly incidence rate of clinical mastitis as the outcome variable was used for the statistical analysis in the second study. The model included recurrent events of clinical mastitis, independent variables with time-varying values and time-dependent effects, and multilevel clustering with different hierarchies. This was the first study investigating associations between the fat-protein ratio and clinical mastitis which used such a complex statistical model. When analyzing associations of the occurrence of clinical mastitis, it is important to include repeated cases because a substantial proportion of all mastitis cases are repeated cases (e.g., Pinzón-Sánchez and Ruegg, 2011; Wolfová et al., 2006). Additionally, the probability of a cow to suffer from clinical mastitis would be expected to be higher if it already had mastitis than if it was never affected by mastitis (Grieger et al., 2014). However, the results of the probabilistic bias analysis in my second study suggested that this effect was sensitive to misclassification of clinical mastitis given the used methods and assumptions. Probabilistic bias analyses are not commonly used in observational studies in veterinary medicine yet. However, they are strongly recommended to assess the systematic error that may occur in field studies (Dohoo, 2014). The fat-protein ratio was not constant over the course of lactation (Buttchereit et al., 2010). Jamrozik and Schaeffer (2012) reported that the differences of the fat-protein ratios between cows with and those without subclinical mastitis were greatest in the first week in milk. Therefore, the fat-protein ratio had to be included in the model as a variable with time-varying value and possibly time-dependent effect. This was possible by using a mixed Poisson model. Analyzing time-to-event data with Poisson regression is innovative in veterinary epidemiology (Stryhn and Christensen, 2014).

To provide dairy farmers information about the losses due to clinical mastitis on their specific farm, a linear mixed model was developed using the statistical software R (R Development Core Team, 2012) which could be integrated in the server-based monitoring software “Daten- und Informationsplattform Tier (DIT)” of the Saxon Dairy Herd Improvement Association. The model was based on the lactation curve model of Ali and Schaeffer (1987) and included short and long term decreases in the daily milk

yield for first and following cases of clinical mastitis per lactation separately. In contrast to the models published so far (e.g., Hagnestam et al., 2007; Schukken et al., 2009), time in milk and time difference to first recognition of clinical mastitis were not included as factors but as quantitative variables. Using quantitative variables allowed to estimate daily milk yield (and losses) and to apply the model to data with only few lactations, i.e., of only one herd. However, the model might lead to unlikely lactation curves in some cases (Figure IV.1). Therefore, checks of the estimated curves would have to be integrated in the automated estimation of herd-specific milk yield loss on the DIT (Zoche-Golob and Spilke, 2013) like the ones described by Zoche-Golob and Köber (2013).

Figure IV.1. Lactation curves predicted by the lactation curve model of Ali and Schaeffer (1987)



Despite these difficulties, the integration of this model into the DIT would provide a useful tool for farmers which would help to assess the losses due to clinical mastitis on their farms as basis for decisions about investments in preventive measures. Additionally, it would allow to compare farms and thus to illustrate the opportunities of a farm to increase its performance by reducing mastitis. However, only milk yield loss due to clinical mastitis was considered in the model. Further models are needed that combine the effects of subclinical and clinical mastitis on milk yield to comprehensively assess milk yield loss due to mastitis on a dairy farm. It will be necessary to consider that the

influences of subclinical and clinical mastitis on milk yield most probably interfere with each other.

The variables for the monitoring of metabolic disorders and the teat condition that were evaluated in this thesis could not be recommended to monitor possible risk factors for mastitis. There was no influence of the teat condition on the occurrence of mastitis. Thus, monitoring the teat condition would be wasted effort in most cases. For a comprehensive and transparent on-farm udder health management, the monitoring variables for the risk factors of interest should be related to the measurement of the actual risk to be controlled (e.g., the incidence rate of clinical mastitis). Milk fat-protein ratios <1.0 and >1.5 were associated with a slightly increased risk of clinical mastitis. However, the ability of fat-protein ratio deviations to predict clinical mastitis was very small and other measures to monitor metabolic disorders as risk factors for mastitis will have to be evaluated. Only variables for the monitoring of two different risk factors for mastitis were investigated. Therefore, further research is needed to generate evidence about risk factors for mastitis and their respective impact on the risk of mastitis, and to evaluate variables that can be used to monitor the risk factors.

The model that was developed to estimate the reduced milk yield due to clinical mastitis could be used to assess herd-specific milk loss and could be integrated in a server-based monitoring software. It provided valuable information as basis for decisions about investments in preventive measures. However, it should be developed further by including the effects of subclinical mastitis on milk yield, too.

V. SUMMARY

Monitoring the udder health in dairy herds

In regions with intensive dairy farming, intramammary infections caused by cow-associated mastitis pathogens became less widespread and intramammary infections with environmental pathogens gained in importance. Environmental mastitis is a multifactorial disease and complex to prevent. Consequently, recommended udder health programs cover not only the milking and mastitis therapy but nearly the whole life cycle of a dairy cow. As herd sizes increase, the continuous monitoring becomes more important for dairy farmers and their veterinarians or consultants to maintain udder health. To avoid unnecessary expenditures for monitoring measures, recommendations are needed how to set up a monitoring system for a farm and which could be helpful indicators. Tools that simplify data analysis for monitoring purposes have to be developed. The overall objective of this thesis was to develop science-based recommendations for different aspects of the monitoring of the udder health on dairy farms on the product and the process level. On the product level, a tool to assess milk yield loss due to clinical mastitis in individual dairy herds was developed and prepared for implementation in a server-based software for monitoring dairy herds. On the process level, variables to monitor the teat condition and distinct negative energy balance as possible risk factors for mastitis were investigated.

Monitoring the udder health of a dairy herd has three functions, which are 1) to describe the actual situation, 2) to evaluate the efficiency of adopted improvement measures and treatments, and 3) to detect emerging problems as early as possible. Therefore, the housing, the feeding and the management of the cows have to be included in the surveillance. Risk-based monitoring of the udder health is characterized on the one hand by focusing on the currently relevant herd-specific risk factors. Consequently, it is a dynamic process. On the other hand, it is effected by a clearly structured approach to prevent a loss of control for lack of attention in any area. All essential decisions and actions are documented to be comprehensible and available for censorious examination. The procedure to establish a risk-based monitoring program for the udder health was summarized in a literature review. It consists of 1) setting goals, 2) a risk analysis, 3) planning of measures and the monitoring, 4) the implementation, and 5) the documentation and regular evaluation.

Machine-milking induced alterations of the teat tissue can be used to evaluate the milking process; they may impair local defense mechanisms, and increase the risk of new intramammary infections. A longitudinal field study was conducted to assess the influence of short-term and long-term alterations of the teat tissue and of the infectious status of the udder quarter on its risk of naturally occurring new intramammary infections, inflammatory responses, and mastitis. Short-term changes of the teat condition are determined by the tissue responses to a single milking like congestions and edema. Long-term changes of the teat condition are the adaptation of the teat tissue to the machine-milking over weeks and are mainly defined by the degree of teat end hyperkeratosis. Short-term and long-term changes of the teat condition of right udder quarters of 135 cows on a commercial dairy farm in Saxony-Anhalt, Germany, were recorded monthly for 10 months using simple classification schemes. Quarter milk samples were collected from all examined quarters at each farm visit. Bacteriological culture results and SCC of the quarter milk samples were used to determine new inflammatory responses (increase from ≤100,000 cells/mL to >100,000 cells/mL between two samples), new infections (detection of a pathogen from a quarter that was free of this pathogen at the preceding sampling), and new mastitis (combination of a new inflammatory response and a new infection). Separate mixed Poisson regression models for new inflammatory responses, new infections, and new mastitis caused by specific pathogens or groups of pathogens (contagious, environmental, major, minor, or any) were used to estimate risk ratios and 95% confidence intervals. The occurrence or non-occurrence of new inflammatory responses, new infections, and new mastitis at time *t* were treated as outcome variables and the teat condition, the infectious, and the inflammatory status at time *t*-1 were used as explanatory variables in statistical analyses to discriminate between cause and effect. There was no effect of any variable describing the teat condition on the risk of new intramammary infections, inflammatory responses, or mastitis. Intramammary infections of the same udder quarter in the preceding month did not have an influence either. According to the results of this study, neither short-term nor long-term changes of the teat condition could be considered as risk factors for mastitis. Therefore, the monitoring of the teat condition cannot be recommended as it would be wasted effort. Further studies are needed to understand if there are certain circumstances or pathogens, when the teat condition becomes more important for the udder health.

Metabolic disorders such as a distinct negative energy balance are plausible risk factors for clinical mastitis. The degradation of body fat increases the milk fat-protein ratio of dairy cows. An increased milk fat-protein ratio is used in practice to monitor metabolic health because it is monthly available for all lactating cows of herds participating in dairy herd improvement tests. In a retrospective cohort study, the association between the test day milk fat-protein ratio and the incidence rate of clinical mastitis was investigated in consideration of repeated cases of clinical mastitis. The objective of this study was to assess the validity of the test day milk fat-protein ratio as a monitoring variable for metabolic disorders as risk factors for the udder health. Herd records of 10 dairy herds of Holstein cows in Saxony, Germany, from September 2005 to September 2011 that compromised of 36,827 lactation periods of 17,657 cows were used for statistical analysis. A mixed Poisson regression model with the weekly incidence rate of clinical mastitis as the outcome variable was fitted that included repeated events of the outcome, updated measurements of independent variables, and multilevel clustering. The lactational incidence of clinical mastitis was 38.2%. In 36.2% and 34.9% of the lactations there was at least one dairy herd improvement test day with a fat-protein ratio of <1.0 or >1.5, respectively. Previous cases of clinical mastitis increased the incidence rate of clinical mastitis. However, given the assumptions that were made about the bias parameters and the methods used for the bias analysis, these conventional results were biased toward the null by the misclassification of clinical mastitis. Fat-protein ratios of <1.0 and >1.5 were associated with higher incidence rates of clinical mastitis depending on the week in milk. The effect of a fat-protein ratio >1.5 on the mastitis incidence rate increased considerably over the course of lactation whereas the effect of a fat-protein ratio <1.0 decreased. Fat-protein ratios <1.0 or >1.5 on the most recent test days of all cows irrespective of their time in milk seemed to be better predictors for clinical mastitis than the first test day results per lactation. The milk fat-protein ratio calculated from dairy herd improvement tests may be a practical trade-off between availability and accuracy for the monitoring of the metabolic health of a dairy herd. However, the results of this study lead to the conclusion that the ability of the test day milk fat-protein ratio to predict clinical mastitis is limited.

To determine the returns on investments in preventive measures that are targeted at improving the udder health, it is important that farmers are aware of the monetary losses due to mastitis. A linear mixed model was developed to estimate the reduced milk yield and the milk loss due to clinical mastitis for a specific herd based on indi-

vidual cows' mastitis and daily milk yield data. The short and long term decrease in the daily milk yield was described by expanding the lactation curve model of Ali and Schaeffer (1987). For calculating the short term drop, the model included the laps of time in days since the mastitis incident as a second-degree polynomial. The coefficients were estimated specifically for the first respectively the recurrent cases of mastitis per lactation. The long term decrease was also modeled separately for the first and the recurrent cases by estimating lactation curves without mastitis as well as for the first and the recurrent cases. By integrating the statistic software R into the processes of the "Daten- und Informationsplattform Tier (DIT)" (a monitoring software for dairy herds of the Saxon Dairy Herd Improvement Association (Sächsischer Landeskontrollverband e. V.)), the estimation of the farm specific model parameters could be largely automated on the servers of the Saxon Dairy Herd Improvement Association. Thereby, the milk yield could be estimated for each day in milk according to the episode number and the time elapsed since the incident or with no mastitis incident, respectively, for a particular period of time in a specific dairy herd. The loss resulting from the reduced performance due to clinical mastitis would be specified by adding up the differences. This information could serve as a valuable basis for management decisions. Online accessible comparisons of milk loss of different farms would illustrate the opportunities of a farm to increase its performance by reducing mastitis.

None of the variables that were evaluated in this thesis could be recommended to monitor possible risk factors for mastitis. Monitoring the teat condition to control the udder health seemed to be wasteful in most cases as the teat condition did not influence the risk of mastitis. The ability of test day milk fat-protein ratios <1.0 or >1.5 to predict clinical mastitis was very small and other measures to monitor metabolic disorders as risk factors for mastitis should be evaluated. However, a useful tool was developed to provide dairy farmers with herd-specific information about milk loss due to clinical mastitis as basis for management decisions.

VI. ZUSAMMENFASSUNG

Monitoring der Eutergesundheit in Milchkuhherden

In Regionen mit intensiver Milchkuhhaltung wurden Euterinfektionen mit kuhassoziierten Mastitiserregern seltener und Euterinfektionen mit Umweltkeimen gewannen an Bedeutung. Durch Umweltkeime ausgelöste Euterentzündungen sind multifaktorielle Erkrankungen und schwierig zu verhindern. Die empfohlenen Eutergesundheitsprogramme umfassen folglich nicht mehr nur das Melken und die Mastitistherapie, sondern fast den gesamten Lebenszyklus einer Milchkuh. Mit steigenden Herdengrößen wird die kontinuierliche Überwachung für Milchkuhhalter und ihre Tierärzte oder Berater immer wichtiger, um die Eutergesundheit der Herden zu erhalten. Um unnötige Ausgaben für Überwachungsmaßnahmen zu vermeiden, werden Empfehlungen benötigt, wie ein herdenspezifisches Monitoringsystem eingerichtet werden kann und welches nützliche Indikatoren sind. Werkzeuge, die die Datenanalyse für das Monitoring vereinfachen, müssen entwickelt werden. Das Ziel dieser Dissertation war es, wissenschaftlich fundierte Empfehlungen für verschiedene Aspekte des Eutergesundheitsmonitorings auf Produkt- und Prozessebene in Milchkuhherden zu entwickeln. Auf Produktebene wurde ein Werkzeug zur Bestimmung des Milchverlusts durch klinische Mastitis in einzelnen Milchkuhherden entwickelt und für die Einbindung in ein serverbasiertes Computerprogramm zum Monitoring von Milchkuhherden vorbereitet. Auf Prozessebene wurden Variablen zum Monitoring der Zitzenkondition und deutlich negativer Energiebilanz als möglichen Risikofaktoren für Mastitiden untersucht.

Das Monitoring der Eutergesundheit in einer Milchkuhherde hat drei Funktionen, nämlich die aktuelle Situation zu beschreiben, die Wirksamkeit von durchgeführten Verbesserungsmaßnahmen und Behandlungen zu bestimmen und auftretende Probleme so früh wie möglich zu erkennen. Deshalb müssen Haltung, Fütterung und Management der Kühe in die Überwachung einbezogen werden. Risikobasiertes Monitoring der Eutergesundheit wird einerseits durch die Konzentration auf die momentan relevanten herdenspezifischen Risikofaktoren bestimmt. Es ist folglich ein dynamischer Prozess. Andererseits ist es gekennzeichnet durch einen klar strukturierten Ansatz, um Kontrollverlust durch mangelnde Aufmerksamkeit in allen Bereichen vorzubeugen. Alle wichtigen Entscheidungen und Maßnahmen werden dokumentiert, um

nachvollziehbar und für spätere Beurteilung verfügbar zu sein. Wie man vorgeht, um ein risikobasiertes Monitoringprogramm für die Eutergesundheit einzurichten, wurde in einer Literaturübersicht beschrieben. Ein risikobasiertes Monitoringprogramm besteht aus 1) der Zielsetzung, 2) der Risikoanalyse, 3) der Planung von Maßnahmen und des Monitorings, 4) der Umsetzung und 5) der Dokumentation und regelmäßigen Evaluation.

Veränderungen des Zitzengewebes durch das maschinelle Melken können zur Beurteilung des Melkprozesses herangezogen werden, lokale Abwehrmechanismen beeinträchtigen und das Risiko von neuen intramammären Infektionen erhöhen. Eine longitudinale Feldstudie wurde durchgeführt, um den Einfluss von kurz- und langfristigen Veränderungen des Zitzengewebes und des Infektionsstatus des Euterviertels auf das Risiko von natürlich auftretenden neuen intramammären Infektionen, Entzündungsreaktionen und Mastitiden zu bestimmen. Kurzfristige Veränderungen der Zitzenkondition sind die Auswirkungen einer einzigen Melkung auf das Zitzengewebe wie Anschoppungen und Ödeme. Langfristige Veränderungen der Zitzenkondition sind Anpassungen des Zitzengewebes an das maschinelle Melken über Wochen und sind hauptsächlich durch die Ausprägung von Hyperkeratosen an der Zitzenkanalöffnung bestimmt. Kurz- und langfristige Veränderungen der Zitzenkondition an den rechten Eutervierteln von 135 Kühen eines kommerziellen Milchkuhbetriebs in Sachsen-Anhalt wurden monatlich über zehn Monate mit Hilfe eines einfachen Schemas dokumentiert. Bei jedem Besuch wurden von allen untersuchten Vierteln Viertelgemelksproben entnommen. Die Ergebnisse der zytobakteriologischen Untersuchungen der Viertelgemelksproben wurden verwendet, um neue entzündliche Reaktionen (Anstieg von ≤100.000 Zellen/ml auf >100.000 Zellen/ml zwischen zwei Untersuchungen), Neuinfektionen (Nachweis eines Mastitiserregers in einem Viertel, der bei der vorangegangenen Untersuchung aus diesem Viertel nicht isoliert wurde) und neue Mastitiden (Kombination von neuer Entzündungsreaktion und Neuinfektion) zu bestimmen. Mittels getrennter gemischter Poissonregressionen wurden relative Risken mit 95% Konfidenzintervallen für neue Entzündungsreaktionen, Neuinfektionen und neue Mastitiden mit bestimmten Keimen oder Keimgruppen (kuhassoziiert, umweltassoziiert, major, minor oder irgendein) geschätzt. In der statistischen Analyse wurden das Auftreten neuer Entzündungsreaktionen, Neuinfektionen und neuer Mastitiden zum Zeitpunkt *t* als dichotome abhängige Variablen und die Zitzenkondition, der Infektions- und Entzündungsstatus zum Zeitpunkt *t*-1 als bestimmende Variablen verwendet, um zwischen Ursache und Wirkung zu unterscheiden. Keine Variable zur

Beschreibung der Zitzenkondition hatte Einfluss auf das Risiko von Neuinfektionen, neuer entzündlicher Reaktionen oder neuer Mastitiden. Auch intramammäre Infektionen des selben Euterviertels im vorangegangenen Monat beeinflussten das Risiko nicht. Nach diesen Ergebnissen können weder kurz- noch langfristige Veränderungen der Zitzenkondition als Risikofaktoren für Euterentzündungen betrachtet werden. Das Monitoring der Zitzenkondition kann folglich nicht empfohlen werden, weil es vergebliche Mühe wäre. Weitere Studien sind notwendig, um herauszufinden, ob es bestimmte Umstände oder Mastitiserreger gibt, bei denen die Zitzenkondition eine wichtigere Rolle für die Eutergesundheit spielt.

Stoffwechselstörungen wie eine ausgeprägte negative Energiebilanz sind denkbare Risikofaktoren für klinische Mastitiden. Massiver Körperfettabbau führt bei Milchkühen zu einer Erhöhung des Milchfett-Eiweiß-Quotienten. In der Praxis wird der Milchfett-Eiweiß-Quotient verwendet, um die Stoffwechselgesundheit zu überwachen, weil er für alle Kühe, die an der Milchleistungsprüfung teilnehmen, monatlich verfügbar ist. Die Beziehungen zwischen dem Fett-Eiweiß-Quotienten am Tag der Milchleistungsprüfung und der Inzidenz klinischer Mastitis unter Berücksichtigung wiederholter Fälle wurden in einer retrospektiven Kohortenstudie untersucht. Das Ziel der Untersuchung war es, zu bestimmen, ob sich der Milchfett-Eiweiß-Quotient aus der Milchleistungsprüfung dafür eignet, auf Stoffwechselstörungen als Risikofaktoren für Euterentzündungen hinzuweisen. Aufzeichnungen von zehn Milchkuhherden aus Holsteinkühen in Sachsen von September 2005 bis September 2011, die 36.827 Laktationen von 17.657 Kühen umfassten, wurden statistisch untersucht. Dazu wurde ein gemischtes Poissonregressionsmodell mit der wöchentlichen Inzidenzrate klinischer Mastitiden als abhängiger Variablen erstellt, das wiederholte Ereignisse der abhängigen Variablen, erneute Messungen unabhängiger Variablen und Gruppierungen auf mehreren Ebenen enthielt. Die Laktationsinzidenz klinischer Mastitiden betrug 38,2%. In 36,2 bzw. 34,9% der Laktationen gab es mindestens eine Milchleistungsprüfung mit einem Fett-Eiweiß-Quotienten von <1,0 beziehungsweise >1,5. Vorangegangene klinische Mastitiden erhöhten die Inzidenzrate klinischer Mastitis. Allerdings erwiesen sich diese Ergebnisse unter den getroffenen Annahmen über die Biasparameter und mit den verwendeten Methoden in der Biasanalyse als zur Null hin verzerrt. Fett-Eiweiß-Quotienten <1,0 und >1,5 standen in Zusammenhang mit einer höheren Mastitisinzidenzrate in Abhängigkeit von der Laktationswoche. Der Einfluss eines Fett-Eiweiß-Quotienten >1,5 auf die Mastitisinzidenzrate stieg im Laktationsverlauf deutlich an, während der Einfluss eines Fett-Eiweiß-Quotienten <1,0 sank. Fett-

Eiweiß-Quotienten <1,0 oder >1,5 in der aktuellsten Milchleistungsprüfung unabhängig vom Laktationsstatus schienen klinische Mastitiden besser vorhersagen zu können als die Ergebnisse aus der ersten Milchleistungsprüfungen pro Laktation. Der Milchfett-Eiweiß-Quotient aus der Milchleistungsprüfung ist wahrscheinlich ein praktikabler Kompromiss zwischen Verfügbarkeit und Genauigkeit zum Monitoring der Stoffwechselgesundheit einer Milchkuhherde, aber die Ergebnisse dieser Studie führen zum Schluss, dass er nur begrenzt geeignet ist, um klinische Mastitiden vorherzusagen.

Damit sie den Gewinn durch Investitionen in vorbeugende Maßnahmen zur Verbesserung der Eutergesundheit ermitteln können, müssen Landwirte die finanziellen Verluste durch Euterentzündungen kennen. Zur Schätzung der reduzierten Milchleistung und des Milchverlusts durch klinische Mastitis in einer bestimmten Herde wurde ein lineares gemischtes Modell erstellt auf Grundlage der Mastitisdaten und täglichen Milchleistung der einzelnen Kühe. Die kurz- und langfristige Reduktion der täglichen Milchmenge wurde durch Erweiterungen des Laktationskurvenmodells von Ali und Schaeffer (1987) beschrieben. Um den kurzfristigen Leistungseinbruch darzustellen, enthielt das Modell die Zeitabstände zum Mastitisfall in Tagen als Polynom zweiten Grades. Die Koeffizienten wurden separat für den ersten beziehungsweise die Wiederholungsfälle pro Laktation geschätzt. Die langfristige Leistungsminderung wurde ebenfalls separat für erste und Wiederholungsfälle abgebildet, indem sowohl Laktationskurven ohne Mastitis als auch mit einer beziehungsweise mehreren Mastitiden geschätzt wurden. Durch die Einbindung der Statistiksoftware R in die Prozesse der „Daten- und Informationsplattform Tier (DIT)“ - eines Monitoringprogramms für Milchkuhherden des Sächsischen Landeskontrollverbands e. V. - könnte die herdenspezifische Schätzung der Modellparameter auf den Servern des Landeskontrollverbands weitestgehend automatisiert werden. Für jeden Laktationstag in einer Herde in einem bestimmten Zeitraum könnte dann die Milchmenge entsprechend der Mastitisfallnummer und der Zeit seit dem Fall beziehungsweise ohne Mastitis geschätzt werden. Der Verlust durch die reduzierte Milchleistung in Folge klinischer Mastitis ergäbe sich dann als Summe der Differenzen. Diese Information könnte als wertvolle Grundlage für Managemententscheidungen dienen. Im Internet verfügbare Vergleiche der Verluste verschiedener Herden würden das Leistungspotential einer Herde durch die Reduktion von Mastitiden verdeutlichen.

Keine der Variablen, die im Rahmen dieser Dissertation untersucht wurden, konnte zum Monitoring möglicher Risikofaktoren für Mastitis empfohlen werden. Die Überwachung der Zitzenkondition, um die Eutergesundheit zu kontrollieren, schien in den

meisten Fällen nutzlos, weil die Zitzenkondition das Risiko für Mastitis nicht beeinflusste. Die Möglichkeiten, mit dem Milchfett-Eiweiß-Quotient aus der Milchleistungsprüfung das Auftreten klinischer Mastitis vorherzusagen, sind sehr gering. Andere Maßnahmen zur Überwachung von Stoffwechselstörungen als Risikofaktoren für Mastitis sollten untersucht werden. Es wurde aber mit dem beschriebenen Computerprogramm ein nützliches Werkzeug entwickelt, das Milchkuhhaltern herdenspezifische Information über den Milchverlust durch klinische Mastitis als Grundlage für Managemententscheidungen bereitstellen kann.

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X. DECLARATION OF INDEPENDENCE

Hiermit bestätige ich, Veit Zoche-Golob, dass ich die vorliegende Arbeit selbständig angefertigt habe. Ich versichere, dass ich ausschließlich die angegebenen Quellen und Hilfen in Anspruch genommen habe.

Tabelle X.1. Eigener Anteil[1] an den Publikationen der vorliegenden Dissertation

	Artikel 1[a]	Artikel 2[b]	Artikel 3[c]	Artikel 4[d]
Studienplanung	+++	+	+++	+++
Datenerhebung	entfällt	+	+++	+++
Datenanalyse	entfällt	+++	+++	++
Verfassen des Manuskripts	+++	+++	+++	+++
Editieren des Manuskripts	++	+++	++	++

[1]Legende: +++: > 70 %
++: 50-70 %
+: < 50 %

[a]ZOCHE, V., HEUWIESER, W., KRÖMKER, V., 2011. Risikoorientiertes Monitoring der Eutergesundheit - Eine Literaturübersicht. Tierarztl Prax Ausg G Grosstiere Nutztiere 39, 88–94.

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[c]ZOCHE-GOLOB, V., HEUWIESER, W., KRÖMKER, V. Investigation of the association between the test day milk fat-protein ratio and clinical mastitis using a Poisson regression approach for analysis of time-to-event data. PREVET (2015) http://dx.doi.org/10.1016/j.prevetmed.2015.06.018.

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