Associations between udder health, udder health management and antimicrobial consumption: Insights into the mechanisms influencing antibiotic usage in German dairy farms

*Franziska Preine[1], Volker Krömker[2], **

[1] Hannover University of Applied Sciences and Arts, Faculty II, Microbiology, Heisterbergallee 10a, 30453, Hannover, Germany; franziska.preine@stud.hs-hannover.de
[2] Faculty of Health and Medical Sciences, Department of Veterinary and Animal Sciences, Section for Production, Nutrition and Health, University of Copenhagen, Grønnegårdsvej 2, 1870 Frederiksberg C, Denmark; volker.kroemker@sund.ku.dk
**Corresponding author: Volker Krömker; Phone: +4520693354; E-Mail: volker.kroemker@sund.ku.dk*

Date submitted:13/07/2022 *Date accepted: 17/09/2022* *Volume/Page(s): 7-15*

Abstract
In the context of increasing antimicrobial resistance of microorganisms, there is growing interest in preventing the development and spread of antimicrobial resistance worldwide through the prudent use of antimicrobials and the reduction in antimicrobial use (AMU). Treatment of mastitis is the main cause for the application of antimicrobial substances in dairy cows. The aim of this study was to investigate associations between udder health, udder health management, and AMU. Factors AMU directly depends on should be found out to achieve the overall goal of optimizing antibiotic consumption without negative effects on animal health. For this purpose, the subclinical and clinical udder health situation of 44 German dairy farms were analyzed at farm-level for the year 2020 using data from the Dairy Herd Improvement (DHI) testing and from herd-specific documentation on clinical cases. A questionnaire was used to describe the udder health management. AMU was measured by the mean number of days under antibiotic therapy due to mastitis per 100 cow years. The results showed that a higher clinical mastitis incidence (CMI) led to a higher AMU. The farm-specific mastitis treatment concept had an influence on the AMU as well. In addition, the actual existence of written treatment protocols was indicated to be associated with higher antimicrobial consumption. However, as more details about the creation, quality as well as the frequency of use of the protocols were not recorded, this result should be interpreted with caution. In conclusion, our study confirms that CMI directly correlates with AMU on dairy farms. Therefore, reducing the number of clinical cases should remain in the focus of farms. Treatment protocols that consider the current state of science and the dynamics of mastitis pathogens on the farm can reduce AMU. They should always be developed with the supervising veterinarian and be regularly reviewed and adjusted. It is also advisable to follow the latest scientific findings and, as far as possible, adapt the treatment concept accordingly, as modern treatment methods can also save on antibiotics.

Keywords: antibiotic, influence, bovine mastitis, dairy cow, mastitis treatment

Introduction
Bovine mastitis remains one of the most common diseases in dairy farming. It not only affects the health of dairy cows but also their production performance [1]. To maintain a healthy, profitable herd, udder health management plays a crucial role. By establishing a high standard of routine work, an improvement in udder health levels can be achieved [2,3]. Both the new infection risk and the duration of existing mastitis can be lowered, leading to a reduction in antimicrobial use (AMU) [4,5]. Regular recording and evaluation of farm-level udder health status are therefore crucial to identify herds that should focus on mastitis prevention [6].
It is a legal requirement to treat diseased animals to ensure animals' welfare, avoid painful diseases like mastitis, and shorten the duration of illness [7]. It is proven that treatment of udder disease is the primary cause of antibiotic treatment in dairy cows [8]. In Europe, for example, almost all clinical cases of mastitis are treated with antibiotics [9]. A major problem here is that any use of antibiotics bears the risk of promoting the development of antimicrobial resistance [10], which currently represents one of the most relevant menaces to public health worldwide [11]. Although the use of antibiotics in food-producing animals is declining and has recently been lower than the use in human medicine, it still contributes greatly to the overall consumption of antimicrobials [12]. There is a growing interest in limiting the development of antibiotic resistance worldwide by reducing the use of antibiotics and using them prudently [11,13]. In Europe, stricter regulations on AMU have only recently been introduced with Regulation (EU) 2019/6, which came into force in January 2022 [14]. This makes it even more crucial for veterinarians and farmers to implement the current state of science and to successfully establish modern counseling and therapy

Table 1: Definitions and benefits of udder health indicators describing the subclinical udder health at herd-level.

Udder health indicator	Definition	Benefits[1]
Udder healthy cows (UH)	Percentage of cows with SCC[2] ≤100,000/mL milk in the present DHI[3] test based on all lactating cows detected by the DHI test	Indicates if udder health requires special attention by farm management
New intramammary infection risk during lactation (NIR LAC)	Percentage of lactating cows with SCC >100.000/mL milk in the present DHI test which were SCC ≤100.000/mL in the previous DHI test	Indicates how well the farm has succeeded in protecting the animals during lactation
Cows with an incurable udder infection (INCUR)	Percentage of all lactating cows having a SCC >700.000/mL milk on three consecutive occasions	Guide to find the right balance between culling and useful life to achieve a long-life span of the cows
New intramammary infection risk during dry period (NIR DP)	Percentage of cows with SCC >100.000/mL milk at the first DHI test after calving from all cows with ≤100.000/mL milk in the last DHI test before drying off	A measure of the quality of work in preventing new infections in the dry period
Cure risk during dry period (CR DP)	Percentage of cows with SCC ≤100.000/mL milk in the first DHI test after calving from all cows with SCC >100.000/mL milk in the last DHI test before drying off	Indicates how well the farm has succeeded in using the dry season as an opportunity to cure existing infections
Heifer mastitis rate (HMR)	Percentage of heifers in milk with SCC >100.000/mL milk at the first DHI test after calving based on all heifers at their first DHI test	Indicates how udder-healthy the animals start their first lactation

[1] [37], [2] somatic cell count, [3] dairy herd improvement test.

tools. A viable option to not only ensure a higher cure rate but also bring about prudent use of antibiotics is the use of an evidence-based mastitis therapy [15]. The basis for these scientifically proven therapy concepts is the prompt delimitation of the cause of the disease, for example through rapid on-farm tests, and a therapeutic decision based on the test result [16]. Performing these rapid on-farm tests as part of an evidence-based mastitis therapy is an effective and proven way to reduce intramammary antibiotics [15,17,18]. Nevertheless, they are not yet widely implemented by farmers, as shown in a study from the Netherlands [19].

To develop further strategies that contribute to a reduction of AMU, it is necessary to examine what AMU directly depends on. To this end, it is important to investigate how udder health and AMU are related and whether they are mutually dependent. There are already studies looking at the relationship between udder health and AMU [20,21]. For example, Nägele et al. examined the connection between udder health and AMU in Switzerland [20]. Their results showed that udder health is related to the incidence of intramammary treatment during lactation, the season of sampling for the dairy improvement test (DHI) to record individual animal cell counts, and the level of expertise of the supervising veterinarian. They also observed that good udder health is possible even with low antibiotic consumption.

Until now, there are no data available in Germany examining how antimicrobial usage and udder health are associated and what AMU directly depends on. The aim of the presented study was to identify factors influencing AMU on German dairy farms. The udder health status and animal health management were recorded and compared with the respective AMU. This information will be used to describe which criteria are decisive for low antibiotic consumption on farms to achieve the overall goal of optimizing antibiotic consumption without any disadvantages for animal health.

Materials and Methods

Farms: The inclusion criteria for the investigated farms were participation in the DHI test, voluntary involvement in this study, and good documentation of disease cases and treatments. Three different groups of farms from different databases were selected. This resulted in a total of 56 farms, a number that was reduced to 44 during the course of the study. The first group comprised 19 farms managed by a veterinary practice in Hesse. The veterinarians there encourage their farmers to keep very detailed records of disease cases and treatments. Nine of those farms were located in Hesse, five in North Rhine-Westphalia, three in Saarland, and one each in Luxembourg and Rhineland Palatinate. The second group included twelve large farms, all of which participated in a research project that required precise documentation on udder health status and the level of AMU. Most of these farms (n=9) were located in central and north-eastern Germany (Brandenburg, Thuringia, Mecklenburg Western Pomerania, Saxony-Anhalt). The remaining farms were located in Lower Saxony and North Rhine-Westphalia (n=3). The third group comprised 25 organic farms from Lower Saxony, Bremen, Hamburg, and Schleswig-Holstein, which are advised by the Competence Centre for Organic Farming „Ökoring e.V." in Visselhövede, Lower Saxony. For the advisory meetings, the results of the monthly milk performance tests and the farmers' documentation on various diseases are compiled.

Antibiotic usage: AMU on farms was measured by the mean number of days under antibiotic therapy due to cases of clinical mastitis per 100 cow years. For this purpose, the number of mastitis cases treated with antibiotics in one year (2020) was first multiplied by the average number of treated days, then divided by the total number of cows and standardized to 100 cow years at risk:

$$AMU = \frac{\text{Number of mastitis cases treated with antibiotics in one year} \times \text{average number of treated days}}{\text{total number of cows in the herd}} \times 100$$

Udder health situation: The subclinical udder health situation was calculated on farm-level for the year 2020 using data from the DHI test

Table 2: Questionnaire subjects on farm-specific treatment practices of clinical mastitis, work routines, and management factors with potential influence on antimicrobial use.

Subjects	Description
Mastitis	Mastitis detection methods Basic rules for the culling of cows with an incurable udder infection available Regular exchange of information between everyone being involved Regular attendance to training courses Use of breeding improvements in udder health
Societal influences	Affection by labor shortage Moral/political/social influences Personal conviction
Treatment	Criteria influencing the way of treatment Treatment protocols available Farm-intern rules for treatment existing Termination of therapy Frequency of use of NSAIDs[1] for clinical mastitis Use of alternative treatment concepts

[1] non-steroidal anti-inflammatory drugs.

Table 3: Questions (n=9) from the questionnaire that have been integrated into the thematic block "mastitis treatment method" and their expressions for treatment methods B1 and B3*.

Main topic	Modern treatment method (B1)	Conventional treatment method (B3)
Culling of cows with an incurable udder infection	Promptly	As late as possible
Use of rapid tests	Yes	No
Start of treatment	When analysis results are available or after consultation with the veterinary practice	Always/often directly after the detection of mastitis
Use of antibiotics	Preferably local or more rarely combined (local + systemic)	Always/often combined or systemic
Initiation of antibiotic therapy	For moderate or severe mastitis cases	Already for mild mastitis cases
Subclinical mastitis	No/rare treatment	Treatment often/always
Extension of treatment duration	Seldom	Often
Dry cow treatment **a) Application of selective dry cow treatment** **b) Standard treatment of dry cows**	a) Yes b) As standard with teat sealants	a) No b) As standard antibiotic dry cow treatment

*For information on the procedure of creating the thematic block: see Figure 1.

and HERDE, a software system for herd management. The DHI test is conducted eleven times a year for each farm by the DHI organization in the respective German states. The test uses single cow samples. The somatic cell count (SCC) is considered a meaningful indicator of udder health and milk quality. In this context, 100,000 SCC/mL milk represents the general threshold for the distinction between a healthy udder and a mastitic one [22]. The evaluated key figures, their definitions, and their benefits are listed in Table 1 as in Hansmann et al. [23]. Arithmetic means were calculated at herd-level for those parameters for the year 2020. Furthermore, standard deviations (SD) were calculated per farm for the proportion of udder-healthy animals and for the new intramammary infection risk during lactation to investigate possible climatic variations. Since the remaining key figures were calculated using a rolling annual average, the standard deviation was not calculated here. The clinical mastitis situation on the farms was calculated using the clinical mastitis incidence rate (CMI). The CMI is an important marker for animal health and welfare and, if recorded regularly, allows the development over time to be recorded and evaluated [24]. It was expressed as the number of clinical mastitis cases per 100 cow years at risk and was calculated as the number of clinical mastitis cases divided by the number of cows at risk in one year and multiplied by 100 cow years. Recurrent cases were not counted, which means that only the new cases were counted for this variable. In accordance with previous studies, a new case was declared after a period of 14 days after the last clinical signs [24,25,26]. All farmers complied with the International Dairy Federation (IDF) standard definition of clinical mastitis in their documentation, which defines clinical mastitis as visible abnormalities in the milk and/or the udder [27].

Animals´ health management and decision criteria for antibiotic treatment: Information on farm-specific treatment practices of clinical mastitis as well as on work routines and management factors with potential influence on AMU was assessed with a questionnaire developed for this purpose (Table 2). The questionnaire included 30 multiple choice questions and six 5-point Likert scales.

Extensive literature research on possible factors influencing the use of antibiotics was conducted in advance. To be as practically oriented as possible, interviews were also conducted in advance with three veterinarians working in the cattle sector and a herd manager and the questionnaire was adapted according to their feedback. It was then pre-tested by two farmers that were not otherwise involved in the study and their comments were also considered in the final formulation. The questionnaire was filled out online by most of the farms. Otherwise, it was answered in person during farm visits or discussed over the phone. Participation in the survey was voluntary and the data were subsequently processed anonymously.

Individual questions from the questionnaire (n= 9) were combined into a thematic block on the topic of mastitis treatment methods (Table 3). The response options of these questions were transformed into variables, each of which was assigned a numerical value between 1 and 5, depending on the degree of agreement with the recommendations based on the evidence from science and literature. The values per farm were then aggregated into a score that was assigned to one of three categories of treatment methods. The lowest score achieved was used as the lower limit for categorization, and the highest score achieved was used as the upper limit (Figure 1). B1 stands for a modern treatment method that largely corresponds to the current recommendations from the literature. Farms in group B2 follow the instructions in the literature to a certain extent but deviate from them in some respects. B3 describes a more conventional treatment method that deviates to a large extent from the current recommendations.

Statistical Analysis: The data were processed and analyzed using the programs Excel (Microsoft Corporation) and SPSS (IBM SPSS 26.0, Chicago, IL, USA) with the dairy herd as the statistical unit. The target value was the AMU of the farms measured as days treated with antibiotics per 100 cow years under risk. Linear mixed models were used to examine associations between AMU (dependent variable) and predic-

Table 4: Results of udder health indicators at herd-level calculated as annual means of monthly herd data (n=44 farms).

Udder health indicator	Mean (%)	Median (%)	SD[1] (%)	Minimum (%)	Maximum (%)	German average 2015[2](%)	Best German farms[3] (%)
Udder healthy cows	58	58	11	36	76	56	74
New infection risk during lactation	20	19	7	10	38	19.8	13
New infection risk during dry period	31	29	12	7	57	26	17
Cure risk during dry period	55	55	13	26	85	55.6	71
Heifer mastitis rate	32	30	13	13	60	31.6	21
Clinical mastitis incidence (CMI)	29	24	21	5	103		

[1] standard deviation, [2] [48], [3] [49].

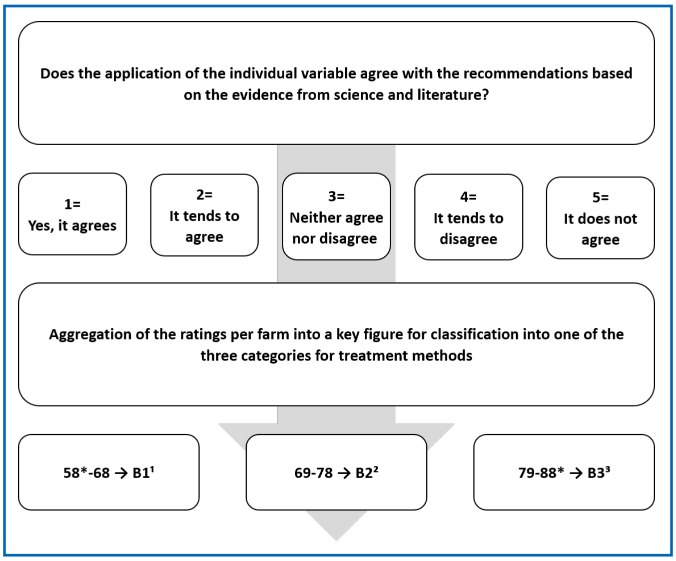

Figure 1: Process diagram for the categorization of different variables from the questionnaire by "mastitis treatment method". * 58= lowest score achieved used as lower limit for categorization, 88= highest score achieved used as upper limit for categorization, [1] modern treatment method, [2] intermediate treatment method, [3] conventional treatment method.

tors (independent variables). The Kolmogorov-Smirnov test was used to test and confirm the normal distribution of the outcome variable. We used the Welch–Satterthwaite equation to calculate the pooled degrees of freedom. The independent variables: farming system, herd size, key figures, mastitis treatment method [categorical variable with three expressions], clinical mastitis cases at herd-level, treatments with NSAID per cow at risk per year, and farm-specific treatment practices for clinical mastitis, work practices, and management factors were subjected to univariable analyses. For inclusion in the multivariable models, variables with $p \leq 0.2$ were retained. To avoid multicollinearity, predictors that correlated strongly with each other ($r > 0.7$) had to be excluded from the model. A stepwise backward procedure was then used to select the final multivariable regression model. Potential risk factors were excluded individually if $p > 0.05$. Potential confounding variables were controlled by observing changes in the regression coefficients. Variables that changed the regression coefficients by more than 20% were considered confounders. No confounding effects were observed. The Akaike information criterion (AIC) was used to evaluate the most optimal model and an AIC closest to zero was used as the final model. All biologic credible two-way interactions were tested in the final model. However, due to lack of significance, these were eliminated again. Model fit was evaluated by checking normality of the residuals. A p-value of ≤ 0.05 was defined as being statistically significant.

Results

Farm demographics: 12 farms were excluded from the final analysis during the study period because they did not respond to the questionnaire or provided data from a year other than the comparison year. Consequently, 44 of the 56 farms originally selected were included in the final study. These included 18 farms from the first group managed by a veterinary practice in Hesse, eight farms from the second group of large farms, and 18 organic farms from the third group. The farms comprised 25 conventionally managed farms and 19 organically managed farms, representing a total of 10,567 cows in the study period of 2020. The mean herd size was 240 cows with a standard deviation of 293 cows. The largest herd included 1490 cows and the smallest 41 cows.

Udder health situation: The udder health parameters based on SCC of the participating farms showed clear differences in all key figures among the farms (Table 4). The mean percentages of udder healthy cows (UH) were 58% and varied between herds from 36% to 76%. The mean new infection risk during lactation (NIR LAC) ranged between 10% and 38%. The arithmetic mean of all farms was 20% for this parameter. The mean new infection risk during the dry period (NIR DP) was 31% and the mean cure risk during the dry period (CR DP) was 55%. For these parameters, the values had a span from 7% to 57% and from 26% to 85%, respectively. The heifer mastitis rate (HMR) was 32% with farms ranging from 13% to 60%. The clinical mastitis situation, calculated using the CMI, also varied greatly among the 44 participating farms and ranged from five to 103 clinical mastitis cases per 100 cow years at risk. The median was 24 and the mean was 29 +/- 21 (Table 4). On some farms, a clear change in udder health during the year could be

Table 5: Results of antimicrobial use (n=44 farms).

Descriptive statistics	Antimicrobial use[2]
Mean	82.45
Median	69.67
SD[1]	58.41
Minimum	4.8
Maximum	250

[1] standard deviation, [2] measured in mean number of days under antibiotic therapy due to cases of clinical mastitis per 100 cow years.

Milk Science International (75) 2022 P. 7-15
ISSN 2567-9538 ; https://doi.org/10.48435/MSI.2022.2

Table 6: Final linear mixed model describing predictors (=independent variables) associated with antimicrobial use (=dependent variable).

Independent Variable	Data Form	Categories	Coefficient	SE[1]	p Value	95% CI[2]
Clinical mastitis incidence	Continuous		0.022	0.0031	<0.001	1.016-1.028
Treatment method	Categorical	B1[3]	-0.714	0.1619	<0.001	0.357-0.673
		B2[4]	-0.429	0.1627		0.473-0.896
		B3[5]	0*			
Treatment protocols available	Categorical	Yes	0.535	0.1582	<0.001	1.253-2.329
		No	0*			

[1] standard error, [2] confidence interval, [3] modern treatment method, [4] intermediate treatment method, [5] conventional treatment method, * redundant coefficient set to zero.

observed by means of a standard deviation of more than 10% or 20%. Most farms, however, showed a rather uniform course of udder health over the course of the year, with a mean standard deviation of 6% for the proportion of udder-healthy animals and 8% for the rate of new infections during lactation.

Antibiotic usage and influencing factors: The results of AMU, measured by the mean number of days under antibiotic therapy due to mastitis per 100 cow years, ranged between 4.8 days and 250 days per 100 cow years. The median was 69.67 and the arithmetic mean was 82.45 days with a very high variability of +/- 58.41 days (Table 5).

Three variables included in the final model were significantly ($p \leq 0.05$) associated with AMU (Table 6). Farms with a higher CMI were also found to have higher AMU. In addition, the mastitis treatment method influenced AMU. Regarding the results of the thematic block on mastitis treatment methods, 18 farms each followed treatment methods B1 and B2 and eight farms applied the conventional treatment method B3. Farms using treatment method B1 had an average AMU of 65 days per 100 cow years. In contrast, farms using method B2 had an AMU of 82 days, and farms following treatment method B3 had an average AMU of 122 days per 100 cow years. Regarding the subclinical udder health of those farms with the more antibiotic-intensive treatment method B3, this did not differ significantly from the udder health of those farms using fewer antibiotics (B1 and B2) (Figure 2). The third influencing factor was the existence of treatment protocols. Farms with treatment protocols in place had a higher AMU with an average of 82 days under antibiotic therapy than farms without treatment protocols. The latter had an average AMU of 75 days.

Discussion

The objective of this study was to investigate the decisive criteria for AMU on 44 German dairy farms. For this reason, the AMU, the udder health status, and the animal health management were recorded to subsequently show possible correlations and influences. Overall, it must be noted that due to the number of evaluated variables being high compared to the number of herds, only major influencing factors could be identified. Furthermore, in the selection process of the farms, emphasis was placed on ensuring that they had accurate documentation of the disease cases and treatments. All farms had been trained over several years by members of a German udder health working group in the management and treatment of udder health disorders and in the documentation of both, allowing for high data quality. As described by Falkenberg et al., only 29.4% of dairy farms in Germany have good documentation of both the occurrence of diseases and their treatment [28]. Furthermore, treatment records from farms are often inaccurate and incomplete [28,29]. Pucken et al. showed that nearly half of the entries in treatment records had at least one important piece of information missing [29]. Including such farms with inaccurate records could have resulted in a high number of unreported cases. In the selection process of the farms, importance was also attached to representing as broad a field of German dairy farming as possible. For this reason, farms with very different characteristics, for example in terms of herd size and production system, were selected for the study. The results of AMU showed an average of 82 days under antibiotic therapy due to mastitis per 100 cow years. In this study, we introduced a new definition to describe AMU on dairy farms, so a classification of our results on AMU cannot be added to the results of other studies. In Germany, it is so far only obligatory for meat producers to determine antibiotic use by recording the frequency of therapy. This requires information on the number and type of animals kept as well as treated, the veterinary drug(s) used, the total amount of drug(s) used, and the number of treatment days [30]. Since this information is not yet obligatory for milk producers, it is not recorded uniformly on the farms.

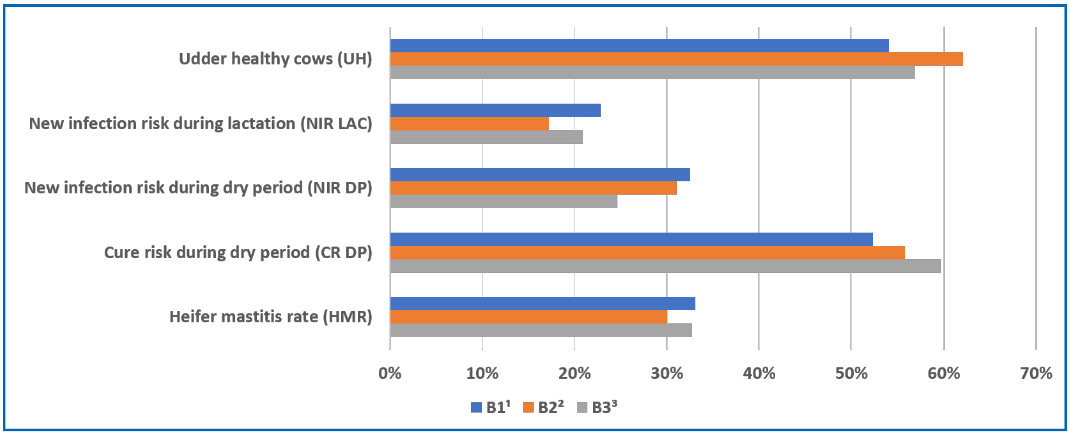

Figure 2: Comparison of udder health among farms with different treatment methods. [1] modern treatment method, [2] intermediate treatment method, [3] conventional treatment method.

Existing definitions for quantifying AMU, such as the standardized ,'Defined Daily Doses'' for veterinary medicine (DDDvet) published by the European Medicines Agency (EMA) [31] could therefore not be used in this study. There are both advantages and disadvantages in using our new method compared to other existing ones. First of all, the required data can be taken either from farmers' records or from herd management systems. This facilitates data collection compared to other methods, such as the garbage can audit, which requires the active participation of producers, regular collection of bin bags, and manual inventory [32]. In our study, data were taken from farmers' treatment protocols. This approach bears the risk that the collected data may be inaccurate and incomplete [29,32]. However, the farms in our study were trained in udder health management for several years and, as described above, were encouraged to keep as complete records as possible, so it can be assumed that an accurate record was kept. Furthermore, the calculation of our new quantification variable is independent of the dosage of the drugs used. The DDDvet is based on average values for dosages from different countries. However, the nationally approved dosages can vary considerably from this and thus lead to misinterpretations [33]. Thus, the calculation of the DDDvet is almost always a compromise. Nevertheless, a compromise was also made with our new method describing AMU on dairy farms, as the average treatment duration of the farms was used to calculate the AMU. Since in some cases, of course, there are deviations from this average duration, the use leads to inaccuracies as well. However, the primary aim of our study was not to precisely quantify antibiotic use but to investigate what antibiotic use depends on. For this reason, an approximation was sufficient to describe it.

The results of this study showed that one of the decisive criteria for AMU was CMI. Thereby, AMU increased with an increasing number of clinical mastitis cases at herd-level. The number of clinical cases used to calculate the CMI in this study included only new cases, as this information was consistent across all three sources. A case detected 14 days after the last clinical signs was considered a new case. This approach is in line with studies from the Netherlands evaluating clinical mastitis, where each clinical mastitis case diagnosed by the farmer was counted as a new case, except for cases that occurred within 14 days in the same quarter [24,25,26]. The fact that no recurrent cases were counted may have influenced the number of clinical cases, considering that many cows develop recurrent clinical mastitis after initial infection [34].

The CMI on the farms investigated in this study was on average 29 clinical mastitis cases per 100 cow years at risk. Santman-Berends et al. described similar results in their study with a CMI of 32.5 in 233 Dutch dairy herds [24]. Other studies, however, showed a much higher CMI [23,35,36]. Hansmann et al. for example, indicated a CMI of 36.6 on 21 organic farms [23]. A CMI of 41.5 was described in a study by Hovi and Roderick for conventional herds [35]. All farms investigated in our study had received udder health training for several years. This could be a possible reason for the lower CMI. As already mentioned above, in Europe, almost all clinical mastitis cases are treated with antibiotics [9]. Furthermore, it is a legal requirement to treat diseased animals [7]. That is why as a logical consequence the use of antibiotic treatments increases with the number of clinical mastitis cases. This fact has been common knowledge for many years and a trend toward lower numbers of clinical mastitis cases is apparent in our study compared to previous studies [35,36]. However, our study findings underline that, despite years of effort, there is still considerable potential for improvement in reducing the number of clinical mastitis cases. The focus of farms should therefore be on reducing NIR both during lactation and the dry period, as this is the basis of mastitis control [7]. This can be achieved through a quality audit of the work routines and framework conditions on the farm, concerning both the husbandry and feeding as well as the milking and drying off of the cows [37].

The mastitis treatment method was another variable that was associated with AMU. On farms using the modern treatment method B1 which largely corresponds to the current recommendations from the literature, AMU was significantly lower. The AMU on farms with B1 was about 50% less in comparison with farms using the conventional treatment method B3. The influence of some parameters that are included in the calculation of the different treatment modalities has already been proven in previous studies and is therefore not discussed here. However, the application of evidence-based therapy concepts as well as the establishment of selective dry cow treatment, which are being applied more and more frequently in Germany, should be emphasized. By establishing on-farm rapid tests for therapeutic decision-making as part of evidence-based mastitis therapy, a significant reduction in antibiotic administration can be achieved [15,17,18]. These also serve as added decision support for farmers for treatment in parallel to veterinary advice. In addition, selective dry cow treatment should be used whenever possible, as it can lead to a reduction in antibiotic consumption [38]. With Regulation (EU) 2019/6, which came into force in January 2022, the prophylactic use of antibiotics in groups of animals was banned. This means that blanket dry cow treatment no longer complies with the requirements of that regulation and instead selective dry cow treatment needs to come into focus [14]. The use of teat sealers, which provide effective protection against new infections during the dry period, plays a decisive role in this respect [37].

The subclinical udder health did not differ significantly among the farms with the different antibiotic-intensive treatment methods. This indicates that subclinical udder health is not necessarily influenced by the treatment method and with a smart treatment concept targeting lower antibiotic consumption, passable udder health is possible. The subclinical udder health situation of the participating farms corresponds to the German average for the most part (Table 4) but is rather unsatisfactory overall. Taking the results of the best German farms as a benchmark, it can be seen that the farms in this study did not achieve comparable results overall. The largest deviations were in the proportion of UH cows (best German farms 74% vs. 58%), the NIR DP (best German farms 17% vs. 31%), and the CR DP (best German farms 71% vs. 55%). In addition, there were clear differences between the farms in terms of how they dealt with weather-related influences, as some farms showed significant fluctuations over the course of the year. This indicates that there were different management and hygiene standards on the farms. For example, some of the farms kept their animals indoors all year round, while on other farms, the animals also had access to pasture. Farms experiencing problems in dealing with variations depending on the climate should adopt more weather-adapted strategies, such as better control of heat stress or dry cover in cubicles [4].

Most of the investigated farms had implemented on-farm treatment protocols. These farms tended to have a higher AMU than those farms without treatment protocols. Contrary to this result, previous studies based on expert opinions of veterinarians from Denmark, Portugal, Switzerland, and the Netherlands have shown that treatment protocols can serve to reduce AMU [39,40]. This highlights that the very existence of treatment protocols does not have significant explanatory power. Its proper application is critical for the beneficial impact of the treatment protocol, which is why it is particularly important that the

Milk Science International (75) 2022 P. 7-15
ISSN 2567-9538 ; https://doi.org/10.48435/MSI.2022.2

content and purpose of the protocols are understood by farmers and farm personnel. The treatment protocols should therefore be written as simply as possible, an objective that is also supported by Mills et al. [41]. They stated that veterinarians' advice to farmers on developing standard operating procedures (SOPs) should focus particularly on the purpose of the SOP, the format that is most appropriate for the farm, and the accountability of employees.

In addition, the respective supervising veterinarians must be involved in the preparation of the treatment protocols. They should also be familiar with the process of preparing the protocols. The present study did not ask who created the treatment protocols and when they were created. Therefore, it cannot be ruled out that the protocols were created without the involvement of skilled veterinarians or had not been revised for some time. Furthermore, the scope and quality of the protocols were not investigated. It has been proven that not every case of clinical mastitis requires antibiotic therapy. In case of non-severe clinical mastitis, only cases caused by Gram-positive pathogens benefit from intramammary antibiotic administration. In contrast, cases of Gram-negative pathogens do not always require antibiotic therapy, as there is a high tendency for self-healing [42,43]. Therefore, if simple or outdated protocols are in place, treatments may not be questioned, and cases may be treated that would not have necessarily required treatment. Frequent review of the protocols can also make it easier for the farmers to verify the need for treatment and thus lead to a greater willingness to treat. A study by Kayitsinga et al. found similar results when treatment records existed [44].

To better capture the effect of different concepts of treatment protocols in future studies, additional criteria should be collected besides the simple question of whether protocols are in place or not. Information on who was involved in the development of the protocols and whether they are regularly reviewed and adapted to the current situation in the herd seems important. It is also useful to check whether all those involved, such as employees, have received instructions in the contents of the protocols and subsequently comply with them. With this information, the quality of the treatment protocols can be better assessed in the future and possible effects, for example on AMU, can be investigated.

Further limitations: As described above, the questionnaire was completed by farmers via three different channels. The majority answered the questionnaire online (73%). The use of web-based surveys is a common practice that, despite known limitations, is widely considered to be a useful tool for investigating general trends [45]. The completion of web-based surveys is easy for participants to schedule, as they can be started at any time. However, response rates to web-based surveys tend to be lower than, for example, paper-based surveys [46]. With the remaining farmers, the questionnaire was processed in person during farm visits (16%) or discussed over the telephone (11%). Here, of course, the response rate was 100%, as the answers were noted directly by the interviewer. Despite the indication that the answers will be treated confidentially and anonymously, there is always a risk of information and self-reporting bias in questionnaire-based surveys [47]. This means that the respondents tend to answer the questions not completely objectively but as they see fit. To avoid this as much as possible, discretion was guaranteed in the personal interviews.

Conclusions

This study shows that the number of clinical mastitis cases at herd-level directly correlates with antibiotic use on dairy farms. The treatment method, as well as the existence of treatment protocols, also influence the level of antibiotic use. The most important leverage point for reducing antibiotic use remains the reduction in clinical mastitis cases. It is also advisable to follow the recommendations based on the evidence from science and literature and adapt the treatment method accordingly as far as possible, as modern treatment methods can also save on antibiotics. In particular, the use of evidence-based therapy concepts as well as the establishment of selective dry cow treatment, methods that are also being used more and more frequently in Germany, should be emphasized here. When using treatment protocols, it should always be taken care that these are adapted to the current herd situation and that they are always drawn up in the presence of the supervising veterinarian.

Disclosure of conflicts of interest

The authors declare no potential conflicts of interest.

Compliance with Ethical Standards

This study has been conducted in compliance with ethical standards.

Acknowledgments

We would like to thank the veterinarians of the veterinary practice in Hesse, those responsible for the research project, the Competence Centre for Organic Farming „Ökoring e.V.", and the farmers for their cooperation and for providing the data.

References

1. Halasa T, Huijps K, Østeras O, Hogeveen H. Economic effects of bovine mastitis and mastitis management: A review. Vet Q, 2007; 29(1):18–31.
2. Dufour S, Fréchette A, Barkema HW, Mussell A, Scholl DT. Invited review: Effect of udder health management practices on herd somatic cell count. J dairy Sci, 2011; 94(2):563-579.
3. Kelly OT, O´Sullivan K, Berry DP, More SJ, Meaney WJ, O´Callaghan EJ, O´Brien B. Farm management factors associated with bulk tank somatic cell count in Irish dairy herds. Ir Vet J, 2009; 62(4):45-51.
4. Klocke D, Schmenger A, Krömker V. Eutergesundheitssituation in großen niedersächsischen Milchviehbetrieben. Der Praktische Tierarzt 101, 2020; Heft 07/2020, 672-683.
5. Dodd FH, Neave FK, Kingwill RG. Control of udder infection by management. J Dairy Sci, 1964; 47(10):1109-1114.
6. Valde JP, Østerås O, Siemensen E. Description of Herd Level Criteria for Good and Poor Udder Health in Norwegian Dairy Cows. J Dairy Sci, 2005; 88(1):86-92.
7. Krömker V, Leimbach S. Mastitis Treatment-Reduction in antibiotic usage in dairy cows. Wiley, Reprod Dom Anim, 2017; 52(Suppl. 3):21-29.
8. Gomes F, Henriques M. Control of Bovine Mastitis: Old and Recent Therapeutic Approaches. Curr Microbiol, 2016; 72(4):377–382.
9. Viora L, Graham EM, Mellor DJ, Reynolds K, Simoes PB, Geraghty TE. Evaluation of a culture-based pathogen identification kit for bacterial causes of bovine mastitis. Vet Rec, 2014; 175(4):89.
10. Christaki E, Marcou M, Tofarides A. Antimicrobial Resistance in Bacteria: Mechanisms, Evolution, and Persistence. J Mol Evol, 2020; 88(1):26-40.
11. Goff DA, Kullar R, Goldstein EJC, Gilchrist M, Nathwani D, Cheng AC, Cairns KA, Escandon-Vargas K, Villegas MV, Brink A, van den Bergh D, Mendelson M. A global call from five countries to collaborate in antibiotic stewardship: United we succeed, divided we might fail. Lancet Infect, 2017; Dis. 17(2):e56–e63.

12. European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and European Medicines Agency (EMA). Third joint inter-agency report on integrated analysis of consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals in the EU/EEA, JIACRA III 2016-2018. EFSA Journal, 2021; 19(6):6712.
13. WHO (Word Health Organization). Global action plan on antimicrobial resistance; 2015 [cited 2022 May 17]. Available from: https://apps.who.int/iris/rest/bitstreams/864486/retrieve.
14. Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. O.J. L 4, 07.01.2019, p.43 [cited 2022 May 12]. Available from: CELEX: https://eur-lex.europa.eu/eli/reg/2019/6/oj/eng.
15. Mansion-de Vries EM, Lücking J, Wente N, Zinke C, Hoedemaker M, Krömker V. Comparison of an evidence-based and a conventional mastitis therapy concept with regard to cure rates and antibiotic usage. Milchwissenschaft - Milk Sci Int, 2016; 69(6):27-32.
16. Mansion-de Vries EM, Hoedemaker M, Krömker V. Aspekte einer evidenzbasierten Therapie klinischer Mastitiden. Tierärztliche Praxis Großtiere, 2015; 43(5):287-295.
17. Schmenger A, Leimbach S, Wente N, Zhang Y, Biggs AM, Krömker V. Implementation of a targeted mastitis therapy concept using an on-farm rapid test: antimicrobial consumption, cure rated and compliance. Vet Record, 2020; 187(10):401.
18. Kock J, Wente N, Zhang Y, Paduch J-H, Leimbach S, Klocke D, Gelfert CC, Krömker V. Udder health effects of an evidence-based mastitis therapy concept in northwestern Germany. Milchwissenschaft - Milk Sci Int, 2018; 71(4):14–20.
19. Griffioen K, Hop GE, Holstege MMC, Velthuis AGJ, Lam TJGM, 1Health4Food–Dutch Mastitis Diagnostics Consortium. Dutch dairy farmers‘ need for microbiological mastitis diagnostics. J Dairy Sci, 2016; 99(7):5551-5561.
20. Nägele F, Pucken VB, Bodmer M, Schouwey S, Schupbach-Regula G, Carmo LP. Analysis of udder health in relation to antimicrobial usage in Swiss dairy farms. Schweiz Arch Tierheilkd, 2019; 161(10):666–676.
21. Stevens M, Piepers S, Supré K, Dewulf J, De Vliegher S. Quantification of antimicrobial consumption in adult cattle on dairy herds in Flanders, Belgium, and associations with udder health, milk quality, and production performance. J Dairy Sci, 2016; 99(3):2118–2130.
22. DLQ (German Association for Performance and Quality Testing). DLQ-Richtlinie 1.15: Zur Definition und Berechnung von Ken¬zahlen zum Eutergesundheitsmonitoring in der Herde und von deren Vergleichswerten, 2014; DLQ guideline 1.15, Bonn, Germany [cited 2022 April 14]. Available from: https://infothek.die-milchkontrolle.de/wp-content/uploads/2018/08/DLQ-Richtlinie-1.15-vom-17.11.2014.pdf.
23. Hansmann VK, Volling O, Krömker V. Udder health in organic dairy herds in Northern Germany. Milchwissenschaft - Milk Sci Int, 2019; 72(3):16-24.
24. Santman-Berends IMGA, Lam TJGM, Keurentjes J, van Schaik G. An estimation of the clinical mastitis incidence per 100 cows per year based on routinely collected herd data. J Dairy Sci, 2015; 98(10):6965–6977.
25. Barkema HW, Schukken YH, Lam TJGM, Beiboer ML, Wilmink H, Benedictus G, Brand A. Incidence of Clinical Mastitis in Dairy Herds Grouped in Three Categories by Bulk Milk Somatic Cell Counts. J Dairy Sci, 1998; 81(2):411-419.
26. van den Borne BHP, van Schaik G, Lam TJGM, Nielen M. Variation in herd level mastitis indicators between primi- and multiparae in Dutch dairy herds. Prev Vet Med, 2010; 96(1-2):49-55.
27. IDF (International Dairy Federation). Suggested interpretation of mastitis terminology. Bulletin of the IDF, 2011; 448, Brussels.
28. Falkenberg U, Krömker V, Heuwieser W, Fischer-Tenhagen C. Survey on routines in udder health management and therapy of mastitis on German dairy farms. Milchwissenschaft - Milk Sci Int, 2019; 72(2):11-15.
29. Pucken V-B, Bodmer M, Lovis B, Pont J, Savioli G, Sousa FM, Schüpbach-Regula G. Antimicrobial consumption: Comparison of three different data collection methods. Prev Vet Med, 2021; 186:105221.
30. Veterinary Medicinal Products Act (TAMG) of September 27th, 2021 (Federal Law Gazette I p. 4530) [cited 2022 April 12]. Available from: http://www.gesetze-im-internet.de/tamg/BJNR453010021.html.
31. EMA (European Medicines Agency). Defined daily doses for animals (DDDvet) and defined course doses for animals (DCDvet); European Surveillance of Veterinary Antimicrobial Consumption (ESVAC). EMA/224954/2016, Veterinary Medicines Division, 2016.
32. Lardé H, Francoz D, Roy J-P, Massé J, Archambault M, Paradis M-È, Dufour S. Comparison of Quantification Methods to Estimate Farm-Level Usage of Antimicrobials Other than in Medicated Feed in Dairy Farms from Québec, Canada. Microorganisms, 2021; 9(5):1006.
33. Kasabova S, Hartmann M, Werner N, Käsbohrer A, Kreienbrock L. Used Daily Dose vs. Defined Daily Dose—Contrasting Two Different Methods to Measure Antibiotic Consumption at the Farm Level. Front Vet Sci, 2019; 6:116.
34. Wente N, Grieger AS, Klocke D, Paduch JH, Zhang Y, Leimbach S, tho Seeth M, Mansion-De Vries EM, Mohr E, Krömker V. Recurrent mastitis–persistent or new infections? Vet Microbiol, 2020; 244:108682.
35. Hovi M, Roderick S. Mastitis and mastitis control strategies in organic milk. Cattle Pract, 2000; 8:259–64.
36. Krömker V, Pfannenschmidt F. Zur Inzidenz klinischer Mastitiden und ihrer Therapie in Milchviehbetrieben des ökologischen Landbaus [Mastitis Incidence and Therapy in Organic Dairy Farms]. In: Heß J, Rahmann G, editors. Ende der Nische, Proc. 8. Wissenschaftstagung ökologischer Landbau, Kassel: kassel university press GmbH; 2005.
37. Krömker V, Klocke D, Leimbach S, Paduch JH, Wente N, Tho Seeth M. Leitfaden: Eutergesundheit bei Stall- und Weidehaltung. Landwirtschaftskammer Niedersachsen, 2018 [cited 2022 April 12]. Available from: https://www.lwk-niedersachsen.de/index.cfm/portal/1/nav/2043/article/32388.html.
38. Hommels NMC, Ferreira FC, van den Borne BHP, Hogeveen G. Antibiotic use and potential economic impact of implementing selective dry cow therapy in large US dairies. J dairy Sci, 2021; 104(8):8931-8946.
39. Carmo LP, Nielsen LR, Alban L, da Costa PM, Schüpbach-Regula G, Magouras I. Veterinary Expert Opinion on Potential Drivers and Opportunities for Changing Antimicrobial Usage Practices in Livestock in Denmark, Portugal, and Switzerland. Front Vet Sci, 2018; 5:29.
40. Speksnijder DC, Mevius DJ, Bruschke CJM, Wagenaar JA. Reduc-

Milk Science International (75) 2022 P. 7-15
ISSN 2567-9538 ; https://doi.org/10.48435/MSI.2022.2

tion of Veterinary Antimicrobial Use in the Netherlands. The Dutch Success Model. Zoonoses and public health, 2015; 62(Suppl. 1):79-87.

41. Mills KE, Koralesky KE, Weary DM, von Keyserlingk MAG. Dairy farmer advising in relation to the development of standard operating procedures. J Dairy Sci, 2020; 103(12):11524-115534.
42. Guterbock WM, Van Eeenennaam AL, Anderson RJ, Gardner IA, Cullor JS, Holmberg CA. Efficacy of intramammary antibiotic therapy for treatment of clinical mastitis caused by environmental patho¬gens. J Dairy Sci, 1993; 76(11):3437-3444.
43. Roberson JR, Warnick LD, Moore G. Mild to Moderate Clinical Mastitis: Efficacy of Intramammary Amoxicillin, Frequent Milk-Out, a Combined Intramammary Amoxicillin, and Frequent Milk-Out Treatment Versus No Treatment. J Dairy Sci, 2004; 87(3):583–92.
44. Kayitsinga J, Schewe RL, Contreras GA, Erskine RJ. Antimicrobial treatment of clinical mastitis in the eastern United States: The influence of dairy farmers' mastitis management and treatment behavior and attitudes. J dairy Sci, 2016; 100(2):1388-1407.
45. Gosling SD, Vazire S, Srivastava S, John OP. Should We Trust Web-Based Studies? A Comparative Analysis of Six Preconceptions about Internet Questionnaires. Am Psychol, 2004; 59(2):93–104.
46. Kongsved SM, Basnov M, Holm-Christensen K, Hjollund NH. Response Rate and Completeness of Questionnaires: A Randomized Study of Internet Versus Paper-and-Pencil Versions. J Med Internet Res, 2007; 9(3):e25.
47. Fadnes L, Taube A, Tylleskär T. How to identify information bias due to self-reporting in epidemiological research. Internet J Epidemiol, 2009; 7:28–38.
48. Behr B, Hachenberg S. Strategisches Eutergesundheitsmonitoring – erste Ergebnisse einer deutschlandweiten Umsetzung. Page 202-208 pigs, bovine, poultry, Proc bpt- Kongress, Hannover 2016.
49. Die Milchkontrolle, Deutscher Verband für Leistungs- und Qualitätsprüfungen e.V. [cited 2022 April 08]. Available from: https://www.die-milchkontrolle.de/milchkontrolle/tiergesundheit/eutergesundheit/.

IISSN 2567-9538 ; https://doi.org/10.48435/MSI.2022.2