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Determinants of antimicrobial treatment for udder health in Danish dairy cattle herds

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ABSTRACT

Societal pressure to limit the use of antibiotics in livestock production systems, including dairy cattle systems, is consistently increasing. To motivate farmers to reduce antibiotic usage, it is important to understand the factors that determine whether a cow will be treated with antibiotics or not. If farmers' usual practices regarding antibiotic treatments are taken into account, they may be motivated to adopt control measures that can facilitate prudent use of antibiotics and are at the same time cost-effective. In this study, we analyzed database recordings of milk yield and somatic cell count from the routine milk recording scheme, clinical registrations of mastitis and PCR results, and cow factors such as days in milk and parity in relation to antibiotic treatments for 518 dairy herds in Denmark. Farm-wise logistic regressions were used to predict antimicrobial treatment based on these factors. The resulting regression coefficients of 422 herds were further analyzed by principal component analysis and clustering to determine the driving predictors for treatment in different groups of farms. The results showed that determinants that were most important for predicting antibiotic treatments vary from one farm to another. Health indicators such as PCR or somatic cell count were most indicative for treatment on some farms, whereas other groups seemed to depend more on production factors (milk yield) or later culling of the cows. This shows that farmers behave differently and differences can be identified in register data. This information can be considered when developing cost-effective herd-specific control measures of mastitis to promote prudent use of antibiotics in Danish dairy cattle farms.

Key words: dairy cattle, antibiotic treatment, mastitis, cluster analysis

INTRODUCTION

Mastitis is one of the most frequent and costly diseases in dairy cattle (e.g., Halasa et al., 2007). Besides impairing animal welfare (Broom, 1991; von Keyserlingk et al., 2009), it is also a major reason for economic losses and prescription of antibiotics in dairy cattle herds (DANMAP, 2014, p. 34; EMA and EFSA, 2017, p. 29). The use of antibiotics in food animals has been a growing concern over the last decades, with increasing consumer awareness regarding this point and its effect on antimicrobial resistance (Ruegg, 2003).

Antimicrobial treatment is an important element in the management of mastitis in dairy herds. It is applied for treatment of clinical mastitis (Steenefeld et al., 2011; Halasa, 2012) and subclinical mastitis (van den Borne et al., 2010), and at dry-off to cure or prevent mastitis cases (Halasa et al., 2009a,b). However, its use must be prudent (i.e., limited to cases in which treatment with antibiotics is necessary while choosing a suitable antibiotic) to reduce the risk of antimicrobial resistance. To optimize antimicrobial usage, it is important to understand antimicrobial treatment patterns for udder health in dairy cattle herds and investigate factors that influence/enhance the treatments. However, it can be challenging to identify what farmers actually do, or why, as such information is not normally registered. Nevertheless, observable factors may give indications and thus may be useful as proxies for behaviors explaining antimicrobial treatment on a farm. Once influential factors are identified for a specific farm, veterinarians and udder health advisors can guide farmers to a prudent and cost-effective selection strategy of cows for treatment, while also taking the farmer's usual selection criteria or management practice into account. This might ease motivating farmers to adopt proposed management programs to improve udder health, thus aiding

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the prudent use of antimicrobials. As blanket dry cow therapy is prohibited in Denmark, an appropriate selection of cows for antibiotic treatment, both during lactation and at dry-off, is expected to have a positive effect on udder health and animal welfare while facilitating prudent use of antibiotics (Scherpenzeel et al., 2016). In Denmark, antimicrobials are prescribed by the herd veterinarian and exclusively distributed through pharmacies. In addition, treatments are normally carried out by veterinarians, but a farmer can have a herd health contract with a consulting veterinarian, allowing him to treat clinical cases of mastitis himself.

The proposed strategies can be developed and examined using, for instance, simulation models adjusted to the herd-specific parameters and with focus on cost effectively optimizing antimicrobial usage. These models can also consider other factors, such as spread of pathogens (e.g., van den Borne et al., 2010; Halasa et al., 2010), and thereby provide a more comprehensive understanding of management and treatment regimens and their expected outcomes, depending on given farm and cow parameters. This knowledge could additionally be used by policy makers when considering new regulations on a national scale.

In Denmark, herd and cow level registrations are collected in the Danish cattle database. They include, in addition to cow ID, for instance, milk yield and SCC from samples obtained through the routine milk recording scheme (6 or 11 times per year), and other recordings as part of a herd health scheme. The data also include recordings about diseases and treatments for individual cows and are being used for, among other purposes, the development of herd health and breeding programs. Its potential for development of herd-specific health management programs can, however, be further exploited.

We investigate if data from the Danish cattle database can be used to predict antimicrobial treatment in relation to udder health management on different farms, and we identify differences between farms regarding treatment and determine which factors are most important for treatment on different farms. This information can be used to develop herd-specific strategies to improve udder health, considering prudent use of antimicrobials and the apparent selection strategy of cows for treatment.

MATERIALS AND METHODS

Data

Anonymized data from 1,500 randomly chosen conventional cattle farms with any milk yield recordings in

Denmark, where at least 90% of the animals are Danish Holstein cows, were retrieved from the Danish cattle database between February 27 and March 1, 2016. At this time, the total number of dairy farms in Denmark was 3,232. Data included information on milk yield, SCC, animal movements, reproduction and calving, dry-off dates, PCR results (from cow-milk samples), clinical registrations, and treatments. Clinical registrations are usually carried out by the veterinarian, but some farmers may also add to the registrations. These registrations include mainly the results of the California mastitis test, but also acute mastitis cases. Only data from Danish Holstein cows were considered in the analyses.

As a first step, data irrelevant for udder health management were removed: clinical registrations and treatment recordings in the database are related to various diseases, but only clinical registrations pertaining to the udder or the mammary gland, registered as the Danish equivalents of “udder” or “mammary gland,” or results from the California mastitis test were kept. Treatments were considered relevant if they were registered as dry-cow treatment, pertaining to the udder or for diagnosed pathogens causing IMI.

As we were interested in treatment patterns in relation to udder health management, in the second step, we split the data set into 3 parts. The first part included 518 herds with available mastitis PCR results, clinical registrations, and treatment recordings in relation to udder health; the second part included 370 herds without PCR but with available clinical registrations and treatment recordings, and the third part consisted of 424 herds with only treatment recordings available.

From the milk recordings of these farms, average milk yields per parity were calculated for every cow and SCC values were log-transformed. Milk yields recorded as 0 or not available (NA), where SCC was also NA, were discarded because they were considered to be automated recordings for cows that were not actually milked (e.g., cows that were just dried off). Log-transformed SCC values that were given as negative infinity were regarded as NA because a SCC of 0 should not be possible. Parity and DIM were calculated according to the given calving dates. Parity was categorized as 1, 2, or ≥ 3 , and DIM were categorized as lactation stages in early (0–30 DIM), mid (31–250), late (251–450), and very late (>450 DIM) lactation. Observations in the last lactation of a cow were marked according to animal movements showing death of the cow, with NA signaling that neither death nor a following lactation could be identified. Treatment registrations within 14 d of a previous registration were considered part of the same treatment (Barkema et al., 1998), except if

a subsequent treatment was registered as dry-off treatment, which was always kept. The PCR was recorded for each tested pathogen (*Staphylococcus aureus*, other staphylococci including CNS, enterococci, *Corynebacterium bovis*, *Escherichia coli*, *Streptococcus dysgalactiae*, *Streptococcus agalactiae*, *Streptococcus uberis*, *Klebsiella* spp., *Serratia marcescens*, *Arcanobacterium pyogenes* and *Peptostreptococcus indolicus*, *Mycoplasma bovis*, *Mycoplasma* spp., *Prototheca* spp., β -lactamase, yeast), but reduced to 1 observation in the data set with the minimum cycle threshold (CT) value. A PCR result with a CT value below 37 was considered positive, as this is the usual cut-off value used in Denmark for antibiotic treatments. Multiple clinical registrations made for 1 animal on the same day with the same result were considered as only 1 recording. As PCR recordings based on milk from the Danish milk recording scheme started in 2009, only data from 2009 onward were taken into account.

Finally, the 3 parts of the data set were transformed in 2 ways to account for possible differences between lactational and dry-off treatments. For lactational treatments, each recorded treatment led to one treatment observation and no-treatment observations were taken for each lactation stage (early, mid, late, very late) without a lactational treatment following in the same lactation/parity. For instance, a cow without treatment would lead to around 3 to 4 no-treatment observations per lactation (depending on when it was dried off), whereas a cow treated in mid lactation would have a treatment observation in mid lactation and may have a no-treatment observation later in lactation. Dry-off treatments were not considered in the data set for lactational treatments, though it was noted if a dry-off treatment occurred at the end of a lactation. For dry-off treatments, there was one observation per parity. In both cases, treatment and no-treatment observations were linked with the corresponding farm and cow, and to the following factors: lactation stage, parity, last average milk yield, and last log-transformed SCC before the observation, as well as information about prior PCR testing (positive PCR or negative/no PCR), clinical registrations (yes/no), and whether or not the observation was in the cow's last parity (yes/no/NA). This is to account for whether the cow was culled or not. Observations in the dry-off treatment data set were additionally linked to information about lactational treatments in the same lactation (yes/no). Observations where parity was unknown were removed.

This led to 1 data set for lactational treatments and 1 for dry-off treatments, each with 3 parts (with PCR and clinical registrations, without PCR, without PCR or clinical registrations).

Statistical Analysis

For the statistical analyses, the data sets were subdivided into smaller data sets, each representing one farm and only including observations of that farm. All computations were done in the statistical computing software R version 3.3.1 "Bug in Your Hair" (R Core Team, 2016), using the additional packages *data.table* (Dowle et al., 2015), *zoo* (Zeileis and Grothendieck, 2005), *lme4* (Bates et al., 2015), and *ROCR* (Sing et al., 2005). Figures were made using the packages *ggplot2* (Wickham, 2009), *ggbiplot* (Vu, 2011), and *dendextend* (Galili, 2015).

Logistic Regression Analysis. To investigate whether average milk yield, log-transformed SCC, PCR, and clinical registration can predict treatment, we performed farm-wise logistic regression. Adding parity, lactation stage, and information about whether or not the cow was in her last lactation as categorical covariates in a multivariable logistic regression to predict lactational treatments in a combined model leads to

$$\begin{aligned} \text{logit}[P(TREAT_i)] = & \beta_{i0} + \beta_{i1}AVGMY_i + \beta_{i2} \log SCC_i \\ & + \beta_{i3}PCR_i + \beta_{i4}CLIN_i + \beta_{i5}PAR_i + \beta_{i6}LAC_i + \beta_{i7}LAST_i \\ & + COW_i. \end{aligned}$$

As observations for dry-off treatments were always taken at the end of a parity, lactation stage was removed in this case, and instead information about whether there was a treatment during the same lactation was added to predict dry-off treatments, leading to

$$\begin{aligned} \text{logit}[P(DCT_i)] = & \beta_{i0} + \beta_{i1}AVGMY_i + \beta_{i2} \log SCC_i \\ & + \beta_{i3}PCR_i + \beta_{i4}CLIN_i + \beta_{i5}PAR_i + \beta_{i6}LTREAT_i \\ & + \beta_{i7}LAST_i + COW_i. \end{aligned}$$

The left-hand sides of the equations, $P(TREAT_i)$ and $P(DCT_i)$, are the probabilities of lactational and dry-off treatment, respectively. *AVGMY* (last average milk yield), $\log SCC$ (last log-transformed SCC), *PCR*, *CLIN* (clinical registration), *PAR* (parity), *LAC* (lactation stage), *LTREAT* (treatment during lactation), and *LAST* (cow's last lactation) are the above-mentioned predictors, and $COW \sim N(0, \sigma_{cow})$ is a random effect of cow. As our analyses were all farm-wise, $i = 1, \dots, 1,312$ was a farm index. For farms without PCR or clinical registrations, the corresponding variables (*PCR*, *CLIN*, or both) were removed.

To evaluate how well the multivariable logistic regression models predicted treatment, models were also additionally fitted on subsets of data, where 10% of the

cows at each farm were randomly excluded when fitting the model and then used for testing model predictions. When predicting treatment for new cows, the model used the average population-level values for the random cow factor. The area under the receiver operating characteristic curve (AUC) was then calculated to evaluate the predictive capability of the models.

Principal Component Analysis. We used the coefficients of the variables obtained by logistic regression in principal component analyses (PCA) to investigate similarities or differences between the farms regarding treatment and treatment determinants. For numerical stabilization, farms with extreme coefficient values were excluded from the PCA. Because not all coefficients were significant, we decided to take the range of the significant coefficients of farms in the same data set and with the same type of registrations (available PCR recordings or clinical registrations) as a scale and considered values as extreme if they were outside of that range. Farms where the logistic regression did not converge were also excluded, leading to 422 farms (325 farms without PCR, 334 without PCR or clinical registrations) included in the PCA on lactational treatment coefficients and 381 farms (274 farms without PCR, 213 farms without PCR or clinical registrations) included in the PCA on dry-off treatment coefficients.

The variables were centered (to 0) and scaled (to unit variance) before PCA was performed.

The rotated regression coefficients were clustered, using Ward's clustering criterion (Ward, 1963) with a cut-off value of 3 clusters. The number of clusters was chosen by a visual inspection of the corresponding dendrograms.

RESULTS

The number of observations per farm differed greatly among farms. In the data set for lactational treatments, numbers ranged from 639 (for farms with PCR recordings; 421 for farms with only clinical registrations; 129 for farms without clinical registrations or PCR) to 15,610 (11,980; 7,795) observations with 79 (34; 2) to 4,969 (3,053; 1,354) cases (treatments) and 424 (310; 70) to 13,090 (8,924; 7,732) controls (nontreatments) across a mean number of 42 (25; 9) to 1,317 (844; 547) cows per farm per year. The corresponding numbers for dry-off treatments were 285 (147; 64) to 10,640 (6,523; 3,775) observations with 1 to 2,348 (2,162; 903) cases and 249 (142; 53) to 9,487 (4,361; 3,770) controls. Fourteen (38; 91) farms had no registered dry-off treatments. Distributions of observations are given in Table 1.

Table 1. Summary statistics for number of positive PCR and clinical registrations, average milk yields (in kg), average SCC (in thousands), total number of cows in parity and lactation groups, and mean number of cows per farm between 2009 and February 2016, split between treatment and nontreatment observations for lactational and dry-off treatments on all farms with PCR and clinical registrations

Item	Treatment observations					Nontreatment observations				
	Minimum	1st quarter	Median	3rd quarter	Maximum	Minimum	1st quarter	Median	3rd quarter	Maximum
Lactational treatment										
PCR	0	1	6	15	306	0	12	128.5	318	3,193
Clinical registrations	0	113.8	269	501	3,713	0	704.8	1,346	2,043	7,618
Average milk yield	24.05	32.32	34.15	36.23	46.71	21.38	30.14	31.72	33.31	42.54
Average SCC	122.7	558.7	715.8	912.4	2,057	137.2	269	330.8	395.6	773.9
Cows in their last lactation	7	116.2	173	258.8	1,393	6	617	783	1,046	3,270
Cows in parity 1	17	110	172.5	270.2	1,839	93	900.8	1,154	1,632	5,580
Cows in parity 2	20	120.2	183	278.8	1,571	67	626.5	815	1,130	3,804
Cows in parity ≥ 3	32	177	271.5	417.8	1,750	66	685.2	931	1,279	4,011
Cows in early lactation	18	105	159	248	1,407	20	576.5	777	1,099	7,652
Cows in mid lactation	26	148	227	356	2,156	131	871.8	1,156	1,611	4,915
Cows in late lactation	3	106	194.5	332.8	2,608	73	687	888	1,221	3,894
Cows in very late lactation	0	7	14	25	271	2	57.25	81	119.8	474
Mean number of cows	9.38	42.41	64.31	90.91	432.4	33.38	156.8	204.4	281.3	1,235
Dry-off treatment										
PCR	0	2	56	174	1,138	0	7	45	132.2	1,013
Clinical registrations	0	71	213.5	389.2	2,282	0	366.8	667	1,046	3,446
Average milk yield	22.54	29.97	32.1	33.91	43.5	20.33	29.4	31.03	32.97	42.2
Average SCC	112.4	290.8	379.8	484.6	2,602	167.7	343.6	429.4	515.4	1,059
Cows in their last lactation	0	2	5	10	115	4	313.2	409	527	1,740
Cows in parity 1	0	44	110	210.2	1,015	75	333.5	458	609.5	3,829
Cows in parity 2	0	46	91	164	732	53	249.2	331	443.5	2,643
Cows in parity ≥ 3	0	47.75	93.5	168.5	756	55	311.2	417.5	584.8	3,015
Cow with earlier treatment	0	70	153.5	294.5	2,121	15	209.2	288	417.5	1,401
Mean number of cows	1	21.64	41.05	70.47	354.6	30.12	108.7	145.2	195.5	1,137

The multivariable logistic regression for lactational treatments, for herds with both PCR and clinical registrations, showed similar significance for all factors on the majority of the farms, though slightly less for parity (Figure 1). The coefficients themselves showed a higher probability of treatment with a higher SCC, higher milk yield or later in lactation (Figure 2). Clinical registration coefficients suggested higher probability for treatment with a clinical registration, whereas PCR coefficients indicated a lower probability for treatment with a positive PCR. Similarly, cows in their last lactation (before culling) mostly had a lower probability for treatment (Figure 2). Parity coefficients were more centered around 0 with a small shift to the left, indicating slightly lower treatment probability for higher parities. This was especially observable in the significant coefficients (Figure 3). For most farms, only some of the coefficients were significant, but for 124

farms (39 farms with PCR and clinical registrations, 47 farms without PCR, 38 farms without PCR or clinical registrations), all coefficients were significant.

Multivariable logistic regression results for dry-off treatments for herds with PCR and clinical registrations were comparable to those for lactational treatments (Figures 4 and 5), though there were more extreme values in the regression coefficients (results not shown). Notable differences could be seen for PCR, where coefficients suggested a higher probability for dry-off treatment given a positive PCR result. A higher probability for treatment was also indicated by coefficients for preceding lactational treatments (Figure 5). On 86 farms (37 farms including PCR, 27 farms without PCR, 22 farms without PCR or clinical registrations), all coefficients were significant.

Model validation by fitting the regressions on 90% of the cows in each model showed very good model fit

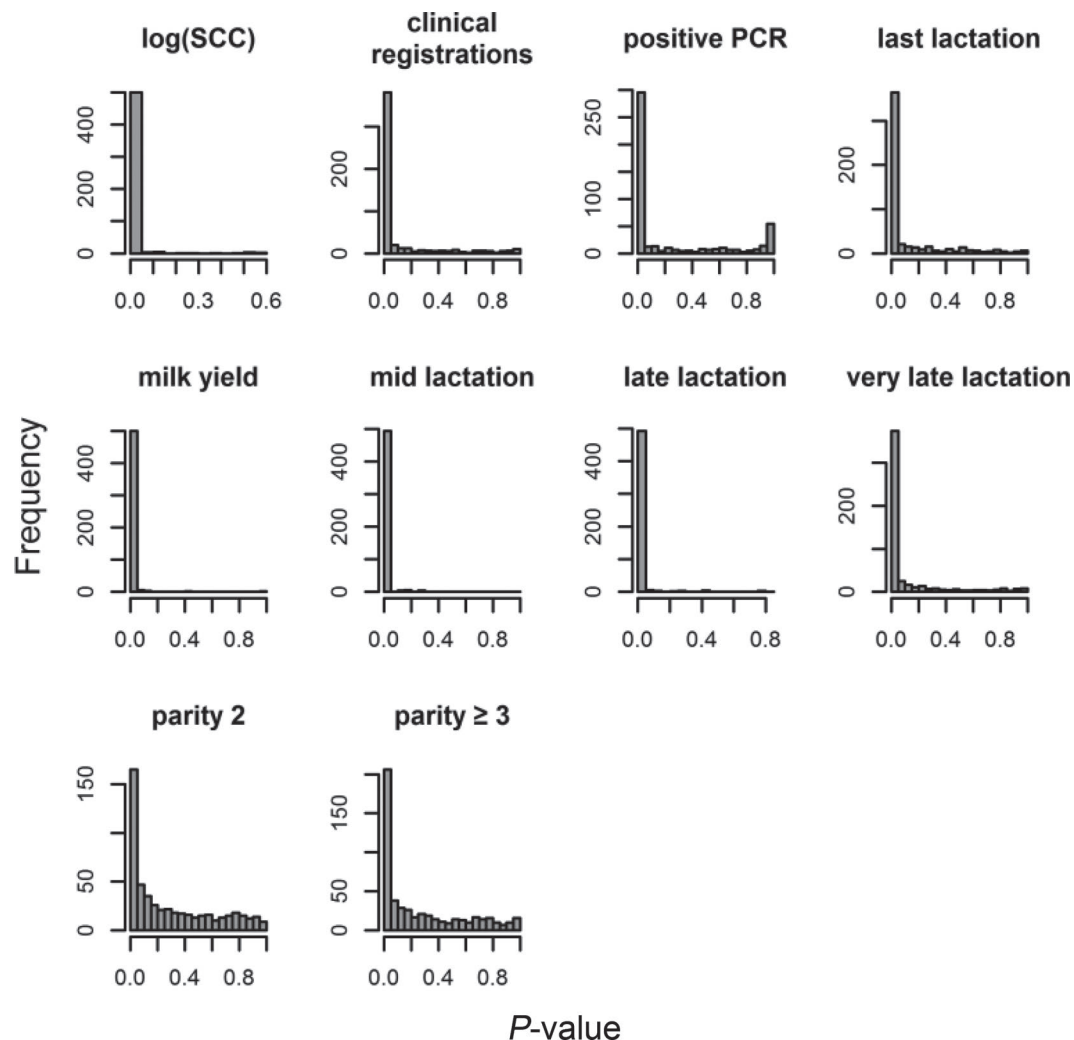


Figure 1. Histogram of P -values in multivariable logistic regressions of lactational treatments for farms with PCR and clinical registrations.

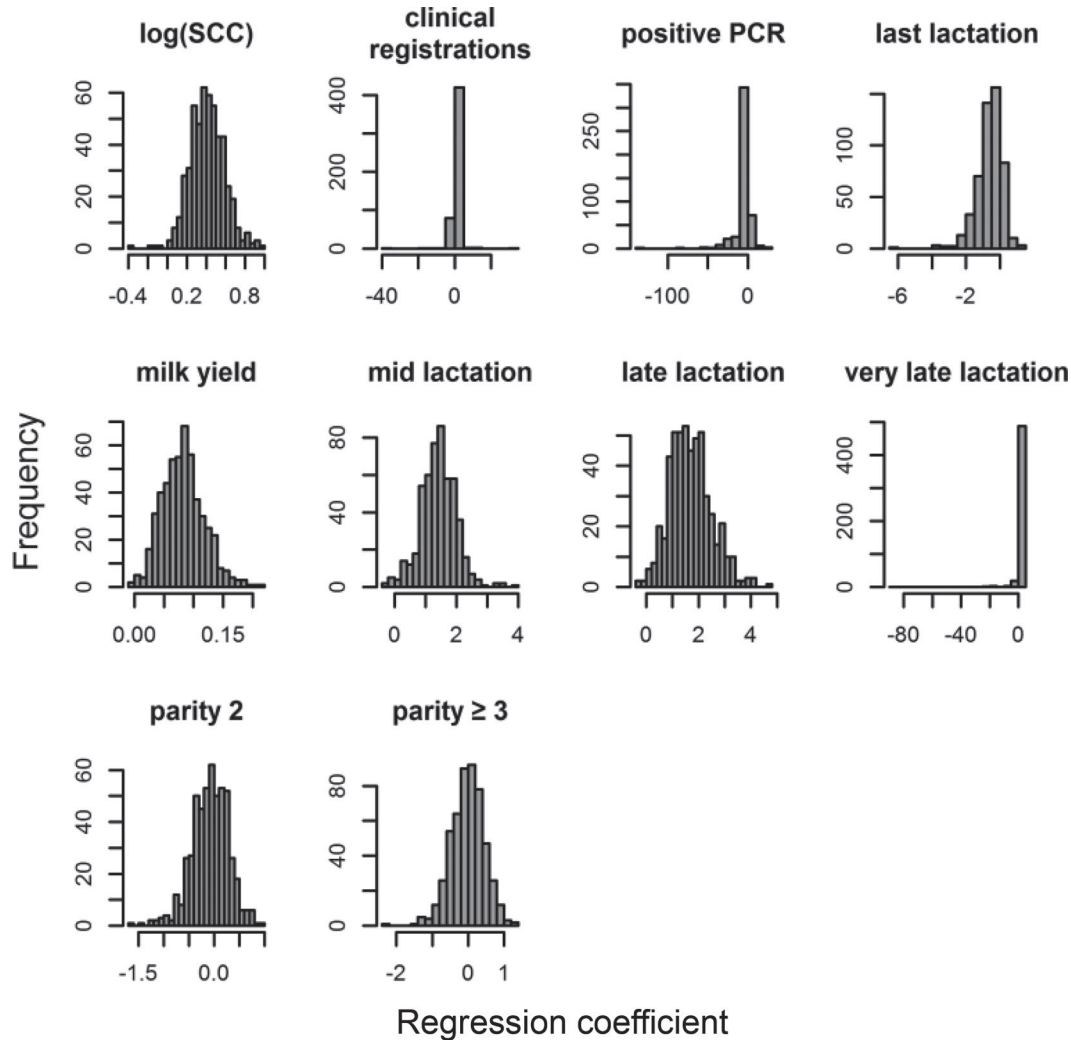


Figure 2. Histogram of coefficients in multivariable logistic regressions of lactational treatments for farms with PCR and clinical registrations. Farms with extreme coefficients (see Figure 3) are removed in further analyses.

for the remaining 10% with the mean AUC at 76% for lactational treatments and 85% for dry-off treatments, and the median AUC at 76.3% (lactational) and 85.8% (dry cow, Figure 6).

The PCA results showed that for both types of treatments the first 2 principal components explain more than 50% of the variance (Figures 7 and 8). These 2 components included all used predictors, although to varying degrees.

Clustering by Ward's clustering criterion on all principal components for lactational treatments showed 3 clusters (Figure 9), one of which was aligned with parity, clinical registrations, and PCR. The second cluster was aligned around average milk yield and lactation stage, and the third cluster was aligned around a cow's last lactation. The SCC seemed to be between this last

and the first cluster (Figure 7). For dry-off treatments, farms seemed to cluster mainly around average milk yield and between parity and a cow's last lactation, with a smaller third cluster aligned with clinical registrations, PCR, SCC, and lactational treatments in the same lactation (Figures 8 and 10). For farms without PCR, clustering for dry-off treatments added several small clusters before more than one big cluster appeared (results not shown).

The included figures show results for farms with PCR and clinical registrations. Specific results of the logistic regression, clustering and PCA for herds without PCR, and herds without PCR or clinical registrations are not shown nor further discussed separately, as they displayed similar trends for both lactational and dry-off treatments.

DISCUSSION

Milk yield recording data, including SCC, are collected regularly on most farms for all cows, leading to near-complete information, whereas PCR has to be transferred and clinical registrations have to be entered into the database manually by the veterinarian or the farmer, who might forget to register this information, sometimes leading to incomplete data or registration errors. Nevertheless, Wolff et al. (2012) investigated the completeness and quality of the national database registers in Denmark, Finland, Norway, and Sweden. The authors found that the Danish register regarding clinical mastitis had the highest quality and around 90% completeness, which increases our confidence in the outcomes of the current study. Still, registration errors do occur, and during data management, we en-

countered some of those such as recordings of dry-off treatments during early lactation, which are most likely treatments for clinical mastitis.

In this study, we conducted untraditional farm-wise logistic regressions because we were interested in both individual farms and in differences between the farms, and not in generic or average estimates corrected for the farm effect. By estimating logistic regression parameters for each farm, we obtained information about individual farms (farm-specific), which could then be used to investigate differences between the farms. We also distinguished between lactational and dry-off treatments, where those were recorded.

Our logistic regression analyses showed that, on many farms, a high SCC and high milk yield are associated with a higher probability of treatment, both for lactational and for dry-off treatments, as is a clinical

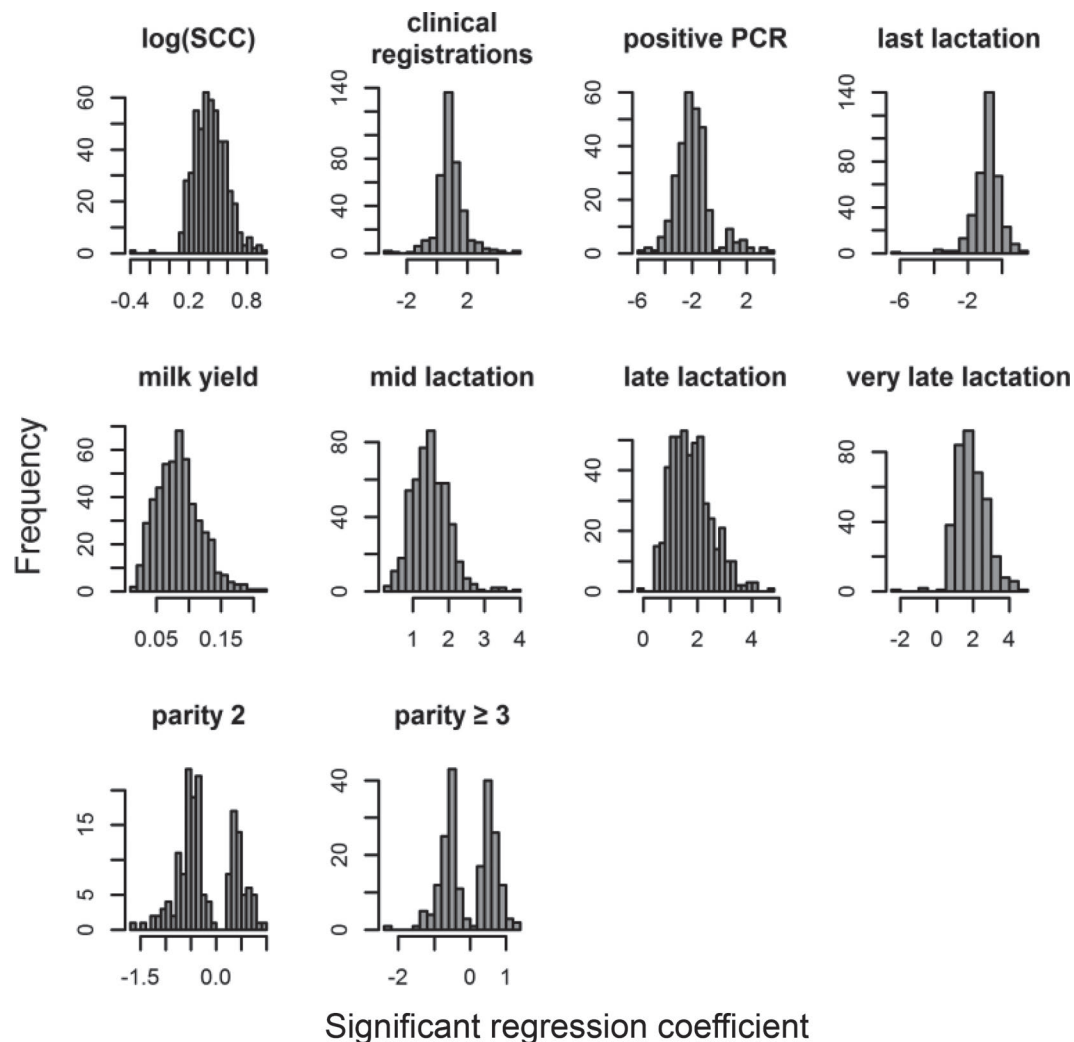


Figure 3. Histogram of significant coefficients in multivariable logistic regressions of lactational treatments for farms with PCR and clinical registrations. The depicted ranges were taken as standard for the coefficient ranges in Figure 2.

registration. Cows that were treated during lactation also had a higher probability for dry-off treatment. It could be that farmers treat cows at dry-off that had a treatment (a mastitis problem) during the lactation, whether they need or do not need the treatment. Earlier studies (e.g., Waage et al., 1998; Zadoks et al., 2001; Steeneveld et al., 2008) have on the other hand shown that high milk production and SCC, as well as previous IMI, are risk factors for clinical mastitis that may lead to antibiotic treatment. These factors may therefore just indicate that there was an IMI (likely to be chronic) that had to be treated. However, it is also expected that farmers would like to keep cows that are performing better than the average cow; therefore, they may rather treat such cows in case of a potential udder health complication to ensure optimal performance of the cows (according to the farmer's belief).

Also, because blanket dry cow therapy is not allowed in Denmark, SCC is one of the main indicators used for selecting cows for testing (using bacterial culture or PCR), subsequently allowing dry-off treatment with antibiotics if the cow is tested positive. If, on top of that, farmers decide to select cows for testing based on whether or not they already had mastitis and mastitis treatment, the associations between dry-off treatments and SCC or preceding lactational treatments could be further explained.

A positive PCR was also associated with a higher probability of dry-off treatment, which can be explained by the fact that Danish legislation allows farmers to use dry cow therapy on PCR-positive cows (Figure 5). On the other hand, a positive PCR seemed to lower the probability for a treatment during lactation (Figures 2 and 3). To find a satisfactory explanation for this, a

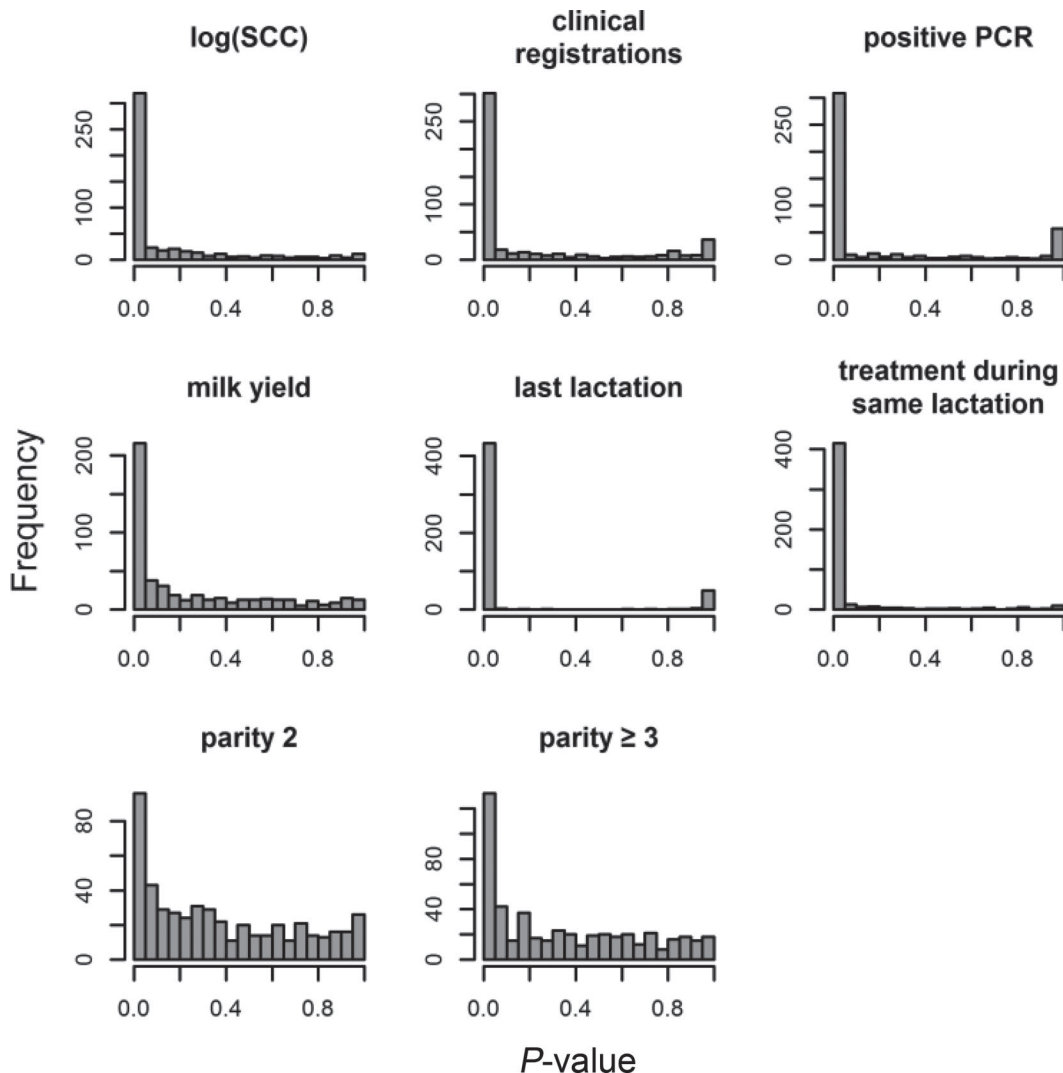


Figure 4. Histogram of *P*-values in multivariable logistic regressions of dry-off treatments for farms with PCR and clinical registrations.

more thorough understanding of when and why farmers decide to use PCR, specifically in relation to lactational treatments, is needed.

For both types of treatment, the regression coefficients showed that cows were rarely treated in their last lactation. This is likely explained by the farmer choosing to cull instead of treating a cow.

The multivariable logistic regression showed different farmer behavior toward treatment when it comes to the parity of the cows (Figures 2, 3, and 5). There seem to be farmers that tend to treat younger cows rather than older ones, as well as farmers that treat the older ones rather than the younger cows. As younger cows are considered the future potential of the farm, the decision to treat instead of cull in case of an udder health complication may not be surprising. On the other hand, a

farmer may decide to keep only higher producing cows and treat those, even if they are older, or hope that younger cows can clear an infection more easily without treatment.

Our results from the PCA and clustering indicated 3 big clusters for lactational treatments (Figure 9) and 2 big and 1 smaller cluster for dry-off treatments (Figure 10). In both cases, 1 cluster covered farms where farmers mostly concentrated on health indicators such as positive PCR, clinical registrations, and SCC. For dry-off treatments, treatments in the same lactation were included in these health indicators, and this cluster was the smallest. Another cluster covered farmers whose decision to treat was based mostly on production factors like average milk yield, and in the case of lactational treatments, DIM, keeping the “more profitable”

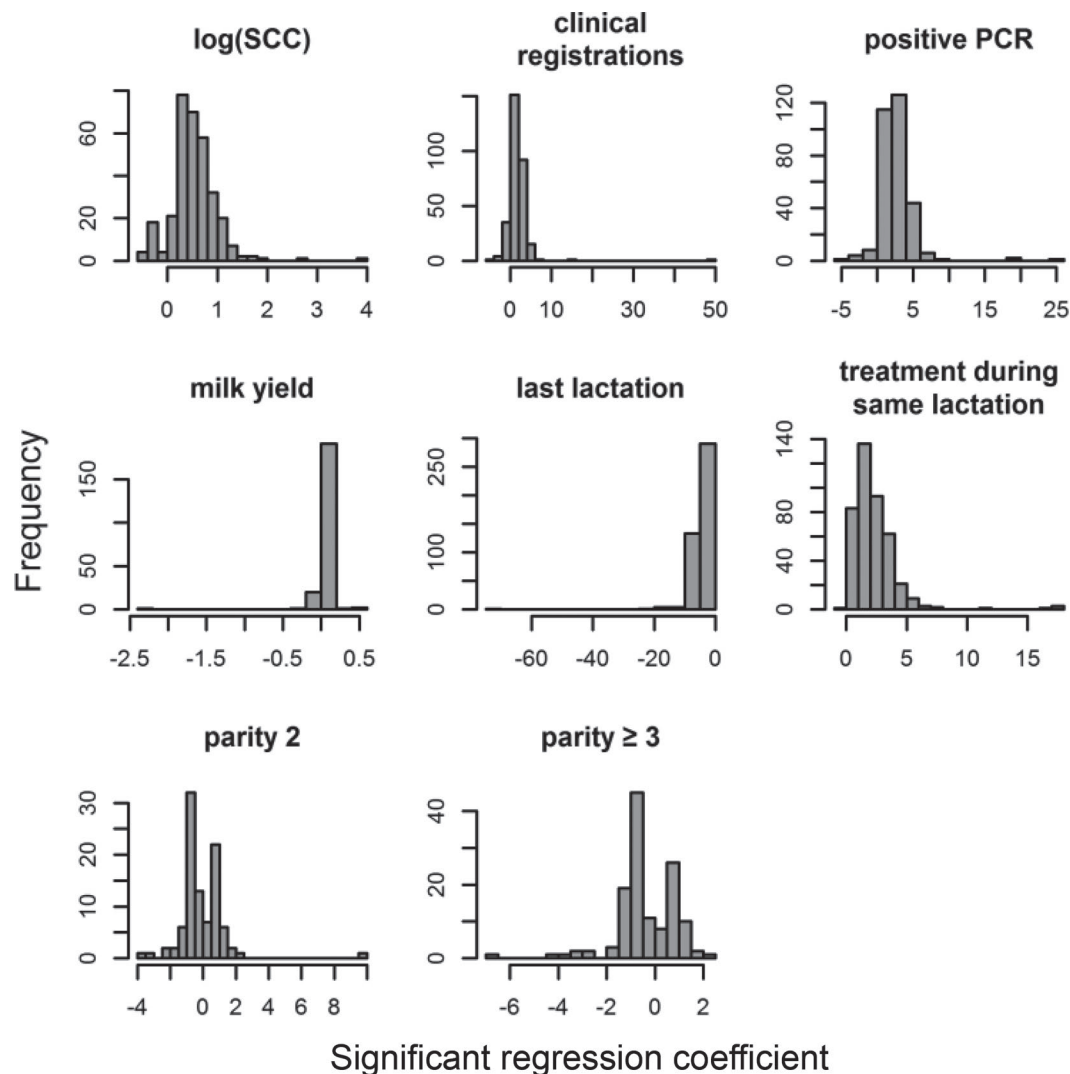


Figure 5. Histogram of significant coefficients in multivariable logistic regressions of dry-off treatments for farms with PCR and clinical registrations. Values outside of the depicted ranges were removed as extreme values.

(high producing) cows. The third cluster for lactational treatments seemed to be centered around a cow's last lactation, also partly including SCC. For dry-off treatments, the third cluster seemed mostly influenced by parity and a cow's last lactation. This may indicate that the farmers' decision to cull instead of treating cows during the lactation is affected by the SCC of the cow, whereas the decision for dry-off treatments may be more affected by the age of the cow.

The decision for treatment may also be influenced by the consulting veterinarian. As we do not account for the veterinarian in our analyses, it is possible that the clustering may be influenced by the herd veterinarian. Further studies could investigate the veterinarian's influence by including the veterinarian as an effect in the model. The farmer himself may also have biased our results by his perception of which cases should receive

treatment, because some farmers may add to the clinical registrations. Still, we expect this bias to be minor because the majority of the cases are registered by the veterinarian.

Cows with clinical mastitis that were not treated but were for instance culled or slaughtered were not considered separately, as culling determinants on different farms were out of the scope of this study. Nevertheless, we tried to adjust for culling by including a binary variable indicating if a cow was in the last lactation. As expected, cows in their last lactation were rarely treated. Further studies focusing on understanding determinants for culling of dairy cows or the more specific relation between treatments and culling may use the methods presented in this study.

We chose a cut-off at a CT value of 37 to define a positive or negative PCR result and we did not consider

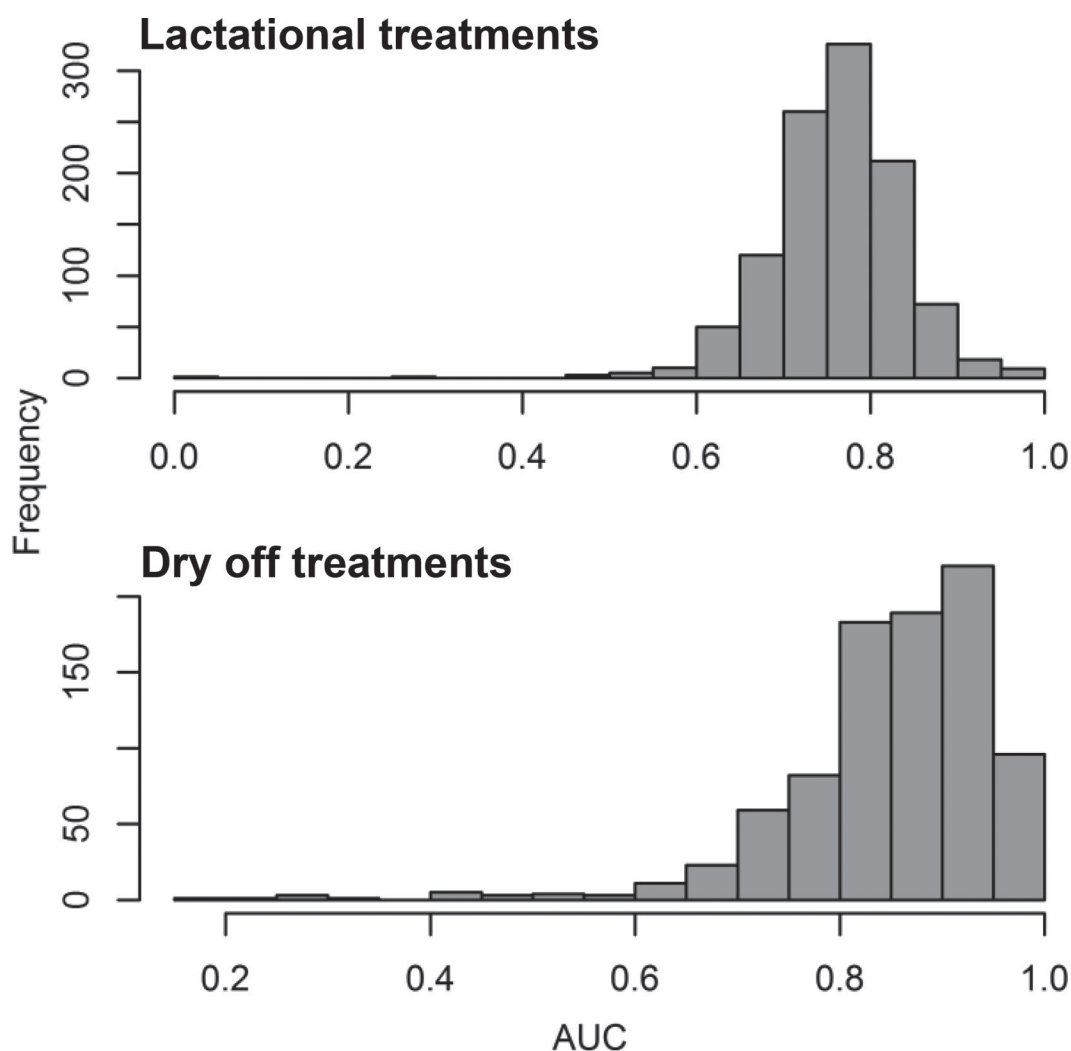


Figure 6. Histogram of area under the receiver operating characteristic curve (AUC) for all farms without extreme coefficients for (a) lactational treatments and (b) dry-off treatments. Model performance was tested on 10% of the cows, which were not included in model fitting.

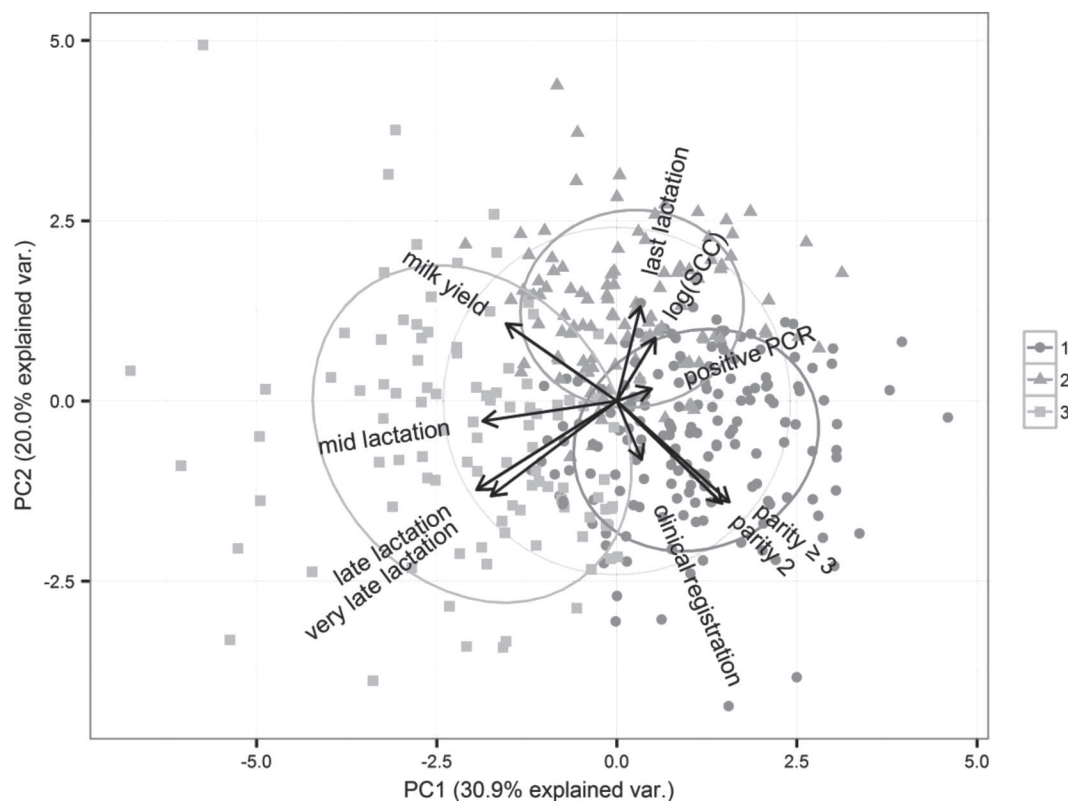


Figure 7. Principal component analysis (PCA) biplot with Ward's clustering criterion for lactational treatments on farms with PCR and clinical registrations. PC1 = principal component 1; PC2 = principal component 2; var. = variance. Color version available online.

other cut-off values, nor the pathogen that the PCR reacted to. The cut-off value of 37 is the value that permits treating cows with antibiotics in Denmark, which farmers generally use. Farmers are allowed to treat cows with antibiotics based purely on a positive PCR result, regardless of the pathogen the PCR reacted to. If they only test cows that they think should be treated, any positive PCR might result in treatment.

Our results clearly show that farmers behave differently. For instance, the results show that health indicators are most indicative for some farms, whereas others use production-related factors (Figures 7 and 8). In addition, variations in the extent of the determinants' effects are clear between farms (Figures 2, 3, and 5). This indicates that a herd-specific approach for udder health improvement with a focus on optimizing the use of antibiotics may be useful. Simulation models could be used to examine and gradually adjust farm-specific udder health management programs under different circumstances (e.g., the level of the mastitis problem in the herd, the causative agent of mastitis, the farmer's way of selecting cows for treatments with antimicrobials, and with different assumptions about the current treatment regimen). This will allow for cost-effective changes of control programs, without having to adopt

a totally different strategy. Thereafter, the information can be communicated by the veterinarian or the milk quality advisors (or both) to provide farm-specific advice not only based on the farmer's statement about his udder health management, but also augmented with available data. Herd-specific control programs that consider a farmer's behavior toward selection of cows for antimicrobial treatments may motivate the farmer to adopt new mastitis control programs resulting in not only improving udder health cost-effectively, but also enhancing prudent use of antibiotics.

CONCLUSIONS

Danish cattle database recordings can be used to find determinants for antibiotic treatment in relation to udder health. Determinants that were most important for predicting antibiotic treatments vary from one farm to another. Health indicators such as PCR or SCC were most indicative for treatment on some farms, whereas other groups seemed to depend more on production factors (milk yield) or later culling of the cows. This shows that farmers behave differently and differences can be identified in register data. Hence, a data-assisted farm-specific approach to improve udder health, which

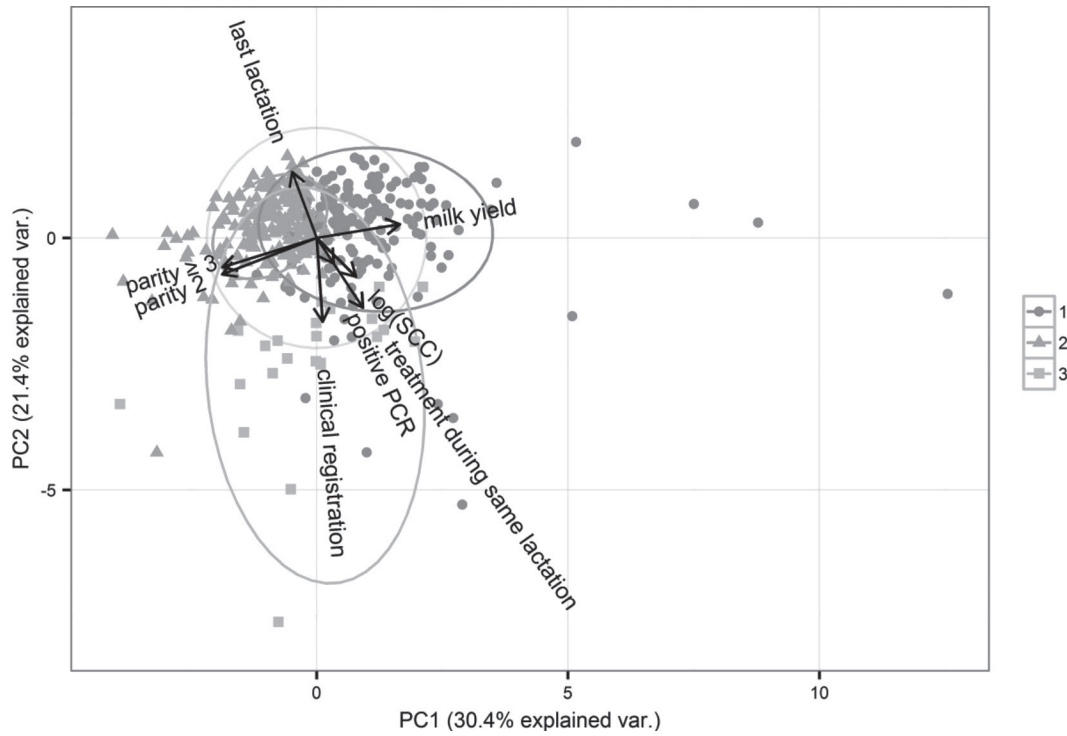


Figure 8. Principal component analysis (PCA) biplot with Ward’s clustering criterion for dry-off treatments on farms with PCR and clinical registrations. One observation [principal component 1 (PC1) = 2.8 and principal component 2 (PC2) = -13.2] in group 3 is not shown in the plot. Var. = variance. Color version available online.

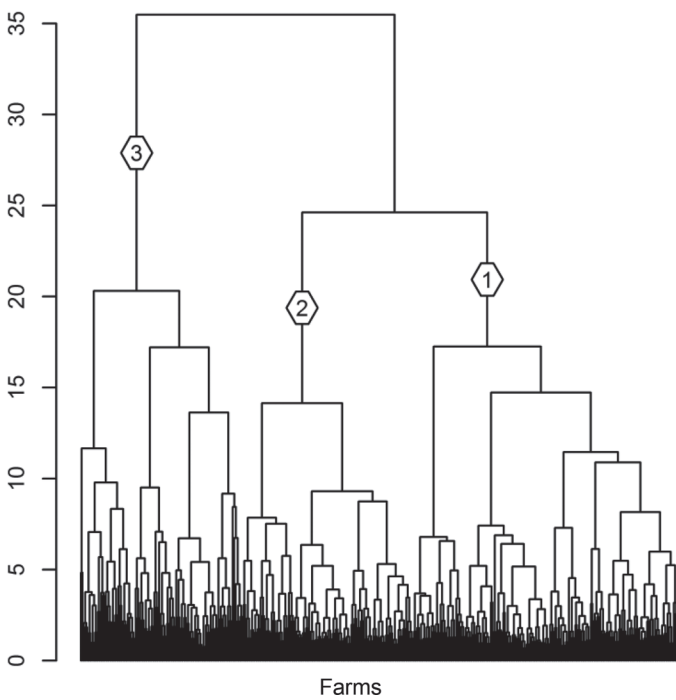


Figure 9. Dendrogram of Ward’s clustering criterion (lactational treatments on farms with PCR and clinical registrations). The clustering height (y-axis) is given in variance units according to Ward’s clustering criterion. Color version available online.

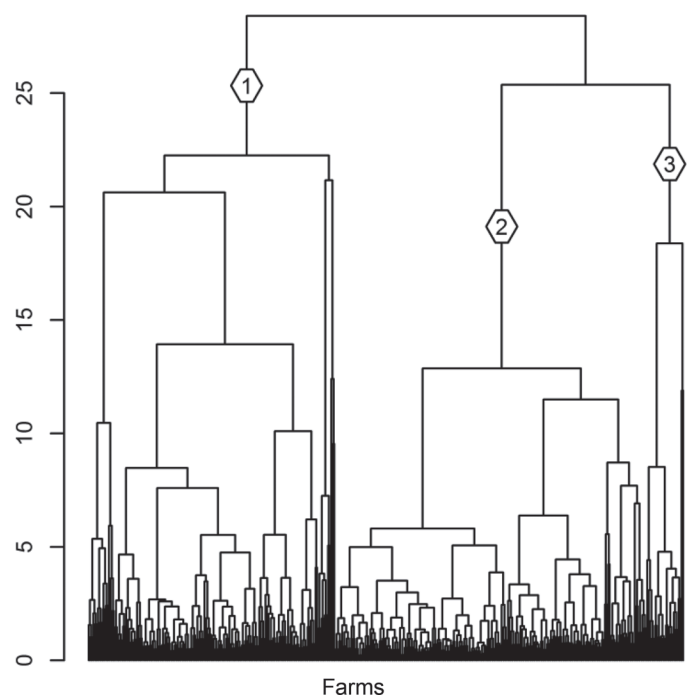


Figure 10. Dendrogram of Ward’s clustering criterion (dry-off treatments on farms with PCR and clinical registrations). The clustering height (y-axis) is given in variance units according to Ward’s clustering criterion. Color version available online.

considers how the farmer selects animals for antibiotic treatments, may prove useful in motivating the farmer to adopt the proposed approach. This would improve udder health and encourage prudent use of antibiotics.

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