J. Dairy Sci. 104:3458–3473
https://doi.org/10.3168/jds.2019-18054

Progression of different udder inflammation indicators and their episode length after onset of inflammation using automatic milking system sensor data

John Bonestroo,[1,2,3]* Mariska van der Voort,[3] Nils Fall,[2] Henk Hogeveen,[3] Ulf Emanuelson,[2] and Ilka Christine Klaas[1]
[1]DeLaval International AB, Gustaf De Lavals väg 15, 147 21 Tumba, Sweden
[2]Swedish University of Agricultural Sciences, Department of Clinical Sciences, PO Box 7054, SE-750 07 Uppsala, Sweden
[3]Wageningen University and Research, Business Economics Group, Hollandseweg 1, 6706 KN Wageningen, the Netherlands

ABSTRACT

In automatic milking systems (AMS), sensors can measure cow behavior and milk composition at every milking. The aim of this observational study of previously collected data was to gain insight into the differences in dynamics of udder inflammation indicators between cows that recover and those that do not recover after detection of an initial inflammation. Milk diversion (milk separated from the bulk tank and thus indicating farmer intervention), conductivity, and somatic cell count (SCC) data from 4 wk before the initial inflammation to 12 wk after the initial inflammation were used to analyze 2,584 cases of udder inflammation. An udder inflammation case was defined as an initial observation of SCC ≥200,000 cells/mL as well as 1 additional SCC measurement >200,000 cells/mL within 10 d after the initial case, among other requirements. The data originated from 15 AMS herds in 6 countries. Four subsets of cows were created based on whether milk was diverted after the initial inflammation and whether the udder inflammation cases recovered, using a 10-d rolling average SCC threshold of 200,000 cells/mL and checking whether this rolling mean was below the threshold within 90 d after the initial inflammation as the indication of recovery. This formed the following subsets of cow lactations: milk diverted–recovered, milk diverted–not recovered, no milk diverted–not recovered, no milk diverted–recovered. Thresholds of 100,000 SCC/mL and 300,000 SCC/mL for the definition of case and recovery were also applied in a sensitivity analysis but with no substantial difference in results. Linear mixed models were used for each subset to study the variation in SCC (natural logarithm of SCC divided by 1,000) and σ-conductivity (natural logarithm of standard deviation of quarter conductivities). When observing the fraction of cows with SCC <200,000 cells/mL in the recovery subsets, most cows recovered within 20 d after the initial inflammation. In the recovery subsets, both σ-conductivity and SCC stabilized, mostly within 3 to 4 wk after the initial inflammation. σ-Conductivity stabilized above the pre-onset level in all subsets and did not show a clear increase in the no-milk-diverted subgroups, whereas SCC stabilized closer to the pre-onset level. Overall, this study indicated a cutoff point between nonchronic and chronic changes in indicators 3 to 4 wk after the initial inflammation for SCC and σ-conductivity.

Key words: mastitis, recovery, conductivity, somatic cell count

INTRODUCTION

Mastitis or udder inflammation is a common production disease in dairy herds, causing compromised animal welfare and high but widely varying economic losses (Hogeveen et al., 2019). Early detection and proper treatment of mastitis is of benefit in terms of milk yield, quality of milk, and cow health (Milner et al., 1997). Research on using sensors for mastitis detection has gained attention (Hogeveen et al., 2010), although the prediction of disease progression and duration has garnered almost no attention in the literature.

In automatic milking systems (**AMS**), sensors continuously measure cow behavior and milk composition for the detection of mastitis (Hogeveen et al., 2010). Because of the increasing number of sensors available on dairy farms, additional cow information is available on a daily or per milking level. This high frequency of measurement creates many novel opportunities that were not possible until quite recently. For instance, these high frequency data have the potential to routinely establish patterns of an udder inflammation episode much more precisely than measurements on DHI test

Received December 13, 2019.
Accepted September 24, 2020.
*Corresponding author: John.bonestroo@delaval.com

days. The time from the point of infection to increased SCC is measured in hours rather than months (Burvenich et al., 1994; Shuster et al., 1996; Kruze et al., 2007; Moyes et al., 2009), and frequent measurement of inflammation indicators is therefore a significant improvement. Having udder inflammation indicator data at every milking could be of high potential benefit for farmers who must decide whether and when to intervene. Farmers could base their decisions on the differences between the patterns of a specific udder inflammation episode and typical patterns of recovered udder inflammation cases. However, practical knowledge of inflammation indicator patterns and the typical inflammation indicator episode duration based on sensor data is lacking. Given that the data are readily available, the potential benefits for farmer decision-making could be large because a potential decision-support system can be widely implemented.

Knowledge about the typical duration and trajectory of an udder inflammation recovery has practical implications. The farmer can decide whether or not to cull a cow when it does not recover after the typical duration of an udder inflammation episode. In addition, definitions of subclinical udder inflammation based on monthly DHI data (e.g., chronicity determined by the past 2 monthly SCC values; as used by St. Rose et al., 2003) are of limited value when a farmer obtains data at every milking. Therefore, specific sensor-based definitions are needed for daily decision-making in sensor-based systems.

Conceptually, udder inflammation recovery or nonchronic udder inflammation can be defined as the cow returning to a healthy state after an udder inflammation episode, as operationalized in terms of SCC in the literature (de Haas et al., 2004). Given that definition, chronicity can be defined as the lack of returning to a healthy state within the period in which recovered cows typically do recover. In the past, researchers used monthly or bimonthly DHI data to study udder inflammation recovery or milk yield losses caused by udder inflammation (Jones et al., 1984; de Haas et al., 2004; Hand et al., 2012). This frequency made it difficult to determine temporal patterns. In contrast, sensors in AMS can measure udder inflammation–related inflammatory indicators, such as conductivity, SCC, and lactate dehydrogenase (LDH), and other milking-related variables (e.g., milk yield, blood presence, and milk flow) at each milking. The analysis of temporal patterns can therefore focus on daily patterns of variables. Fogsgaard et al. (2015) looked at the recovery phase of udder inflammation in general and for different pathogens using AMS data. They concluded that udder inflammation has large effects on milking frequency, LDH activity, and milk yield. However, the patterns of conductivity- and SCC-based measures remain to be explored.

The overarching aim of this observational study was to gain insight into the differences in the progression of inflammation indicators after the initial onset of udder inflammation, as indicated by an increase in SCC between cows that recover and cows that do not recover on commercial dairy farms. More specifically, the study explored sensor measurements of SCC and conductivity in terms of episode length (the time until the inflammation indicator stabilizes; i.e., revolves around a constant mean) after the initial onset of udder inflammation, and whether the level after the initial udder inflammation is equal to that before the initial udder inflammation. This knowledge can be used to build new groundwork for the definitions of chronic and nonchronic udder inflammation cases using daily available sensor data.

MATERIALS AND METHODS

Data Collection

Data of 15 AMS herds located in Belgium, Canada, Germany, the Netherlands, Scotland, and Sweden were retrieved from a database of DeLaval International AB (Tumba, Sweden). The data covered a period from January 4, 2016, to March 14, 2019, although not all farms began reporting on January 4, 2016. The herds were selected based on the presence of an AMS (VMS series, DeLaval International AB) to measure conductivity, an Online Cell Counter (**OCC**; DeLaval International AB) to measure SCC, and having documentation on whether milk from individual cows was diverted from the bulk milk tank. Because this was an observational study using previously collected data, we did not have any information on farmers' approach toward milk diversion. Consequently, we could not control for differences in milk diversion strategies or the diagnostic skills to detect and treat inflammation by the farmer. The average daily milk yield per cow varied between 27.9 and 39.9 kg/d between herds, with a mean of 32.2 kg/d (Appendix Table A1).

The following variables were gathered from the AMS management software and included in this study:

- Milk diversion, defined as whether milk on that day did enter the bulk tank to be sold (1) or not (0). Because the farmer diverted milk away from the bulk tank with consumable milk, the diversion is likely due to an intervention in, for example, a mastitis case (Bonestroo et al., 2020). We used milk diversion as a proxy for farmer intervention and to separate cases where farmers have likely detected and intervened in the case.

- Mean conductivity of the milking quarters during milking. This was used to calculate σ-conductivity, defined as the natural log of the standard deviation of the mean quarter conductivities within cow over the total milk produced at each milking.
- SCC, in 1,000 cells/mL as measured by an OCC.
- DIM.
- Parity, with 2 categories: primiparous (0) and multiparous (1).

The natural logarithm transformation was applied to σ-conductivity and SCC to obtain approximately homoscedastic and normally distributed residuals in the linear mixed model.

Preparation of Data

Milking level observations of SCC, σ-conductivity, and the diverted milk indicator were aggregated to a daily level by taking the maximum value of these values on a given day. Every observation below 10 DIM of every lactation was removed. This was an average of DIM removal thresholds used by other authors (Hand et al., 2012; Dalen et al., 2019).

Below, we define the episodes and their requirements. An overview of these definitions can be seen in Figure 1. The start of an udder inflammation episode during lactation was defined as the first observation within lactation of an increased SCC (as measured by OCC) ≥200,000 cells/mL. This start of the udder inflammation episode was defined as the "initial inflammation" in this study. The data from 4 wk before the initial inflammation and as much as was available until 12 wk after the initial inflammation was used for analyses, and this time period was defined as the "udder inflammation episode sequence." Next, a set of requirements was imposed. First, to counter the possibility of a false-positive initial inflammation detection, the initial inflammation needed to be combined with one or more SCC measurements ≥200,000 cells/mL (Dohoo and Leslie, 1991; Smith et al., 2001) within all measurements taken in the 10 d after the initial inflammation. This 10-d window was chosen because we expected that SCC would be measured on multiple days in the first 10 d after the initial inflammation. It is important to note that the initial inflammation (d 0 in our analysis) remained the first day when SCC increased above or equal to 200,000 cells/mL. Farmers can choose the OCC sampling settings; for example, following the default algorithm of the system or requiring daily measurements of each cow. Lactations without an increased SCC within 10 d after the first initial inflammation were completely removed from the data set, because we could not confirm the start of the udder inflammation episode, and possible later episodes may therefore be part of the same unconfirmed episode. Second, lactation cycles were removed when 80 d or fewer with data were recorded within the first 10 to 100 DIM, to ensure that we had records of at least the start of each selected lactation to minimize the risk that the first initial inflammation that occurred earlier in lactation was not in the data sample.

In total, 7,302 of 7,902 lactations had cases of initial inflammation according to the case definition of an

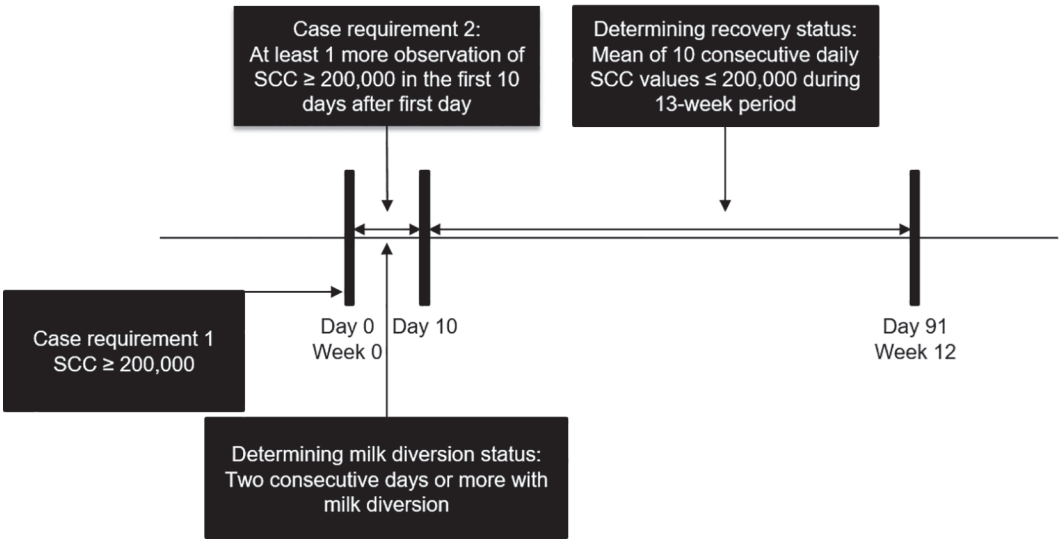

Figure 1. A graphical overview of the case definitions as used in this study. SCC is in cells/mL.

OCC observation ≥200,000 cells/mL. Next, 4,331 of the 7,302 udder inflammation episodes had an additional OCC SCC observation ≥200,000 cells/mL within 10 d after the initial inflammation. Finally, 2,584 udder inflammation episodes of the 4,331 originated from lactation cycles in which more than 80 day-observations during the first 10 to 100 DIM were recorded and thus were retained for analysis.

Because treatment records were not available from all herds, we chose to use milk diversion as an approximation of a farmer intervention related to a mastitis episode (Bonestroo et al., 2020). Milk diversion was defined as diversion of milk for at least 2 consecutive days within the 10 d after the initial inflammation. A period of 2 d was chosen to avoid including automatic milk diversions made by the AMS itself based on sensor thresholds. We assumed that when milk was diverted for at least 2 d within 10 d of the initial inflammation, a cow was confirmed by the farmer as having mastitis and having diverted milk because (a) milk was deemed as not consumable, (b) the cow was treated with antibiotics, or (c) both. If there was no diversion after an episode according to our definition of an udder inflammation episode, we assumed that the farmer did not intervene. Occasionally, some days of some cows with an udder inflammation episode, milking data, and milk diversion data could be missing. The missing values most likely indicated that a cow was milked outside the AMS during an udder inflammation episode. In these cases, we replaced the milk diversion status with the value of the previous day with complete registrations. This was done solely to determine milk diversion status and the imputed version of milk diversion was not further used in the data analysis.

Recovery was defined as a decrease in SCC (measured by the OCC) to a healthy level after an initial increase of SCC to an unhealthy level, as done by de Haas et al. (2004). The threshold between a healthy and an unhealthy level was defined as 200,000 cells/mL (Smith et al., 2001). However, a gray area exists between 100,000 and 199,999 cells/mL, according to the National Mastitis Council (Smith et al., 2001). To evaluate the influence of the chosen threshold, we also tested 100,000 and 300,000 cells/mL in the sensitivity analysis. More specifically, recovery from an udder inflammation episode for an individual cow was defined as the individual cow having a rolling mean SCC <200,000 cells/mL (Smith et al., 2001) for 10 consecutive days within 12 wk after the initial inflammation in the episode sequence. The rolling mean was only calculated when, during the 10-d window, at least 5 d with SCC measurements were available. In the case where fewer than 5 d with SCC measurements were available in the 10-d window, the recovery status was determined as undefined and not regarded as recovered within the 10-d window.

Using the recovery definition and milk diversion status after the initial inflammation, the data set was split into 4 subsets of cows: (1) no diverted milk–no recovery, (2) diverted milk–no recovery, (3) no diverted milk–recovery, and (4) diverted milk–recovery.

Statistical Analysis

The effects of predictor variables on SCC and σ-conductivity were analyzed using a multivariable linear mixed model for each subset with DIM, parity, and weeks since initial inflammation as covariates and a random effect of a specific cow lactation (LactationID) and a random effect of a specific herd (HerdID); HerdID and LactationID indicate the identity of the herd and specific cow lactation number for a specific cow (e.g., cow 12 in its second lactation). Weeks since initial inflammation was a categorical variable with 17 levels (once per week from 4 wk before until 12 wk after the initial inflammation). Parity was a categorical variable coded for primiparous (0) and multiparous cows (1). The analysis used the daily data to estimate the effects of being several weeks before or after initial inflammation to analyze the data (Fogsgaard et al., 2015) to avoid unnecessarily complex models in the number of daily parameters that would need to be estimated.

The models for Y (i.e., SCC or σ-conductivity) took the following form:

$$Y = \text{constant} + \sum_{i=-4}^{12} \left(week\ since\ alert_i\right) + parity + DIM + random\ intercept\ of\ LactationID\ in\ HerdID + random\ intercept\ of\ HerdID,$$

where i is the week number relative to the week in which the initial inflammation was observed. Estimated marginal means were assessed for the weeks since the initial inflammation while evaluating all other covariates at mean level. Different interactions and quadratic terms were tried but they had no substantial effect on the estimated marginal means and were therefore omitted. Random effects of lactation of a specific cow and herd were included in the models as nested random intercepts (LactationID in HerdID and HerdID) and a first-order autoregressive correlation structure was used in line with Fogsgaard et al. (2015). The assumptions of homoscedasticity and normality of residuals were checked using fitted value residual plots and quantile-quantile (qq) plots. The linear mixed models were esti-

mated using nlme 3.1–137 (Pinheiro et al., 2019) using REML in R 3.5.1 (https://www.R-project.org/).

The robustness of the results subject to the exact values for these thresholds described above (Figure 1) was tested in a sensitivity analysis by changing the SCC threshold to 100,000 and 300,000 cells/mL for the recovery definition and case requirements (requirements 1 and 2) in case definition (see Figure 1) separately. We also changed the days in requirement 2 of the case definition from 10 d to 5 and 20 d (see Figure 1). Furthermore, the recovery definition was altered by changing the consecutive days from 10 d to 5 and 20 d during which the rolling mean SCC should be <200,000 cells/mL to determine recovery. The milk diversion status definition was changed from 2 d of milk diversion to 5 consecutive days of milk diversions in the first 10 d after the initial inflammation. Last, we reran the analysis for the 2 herds with the largest number of episodes to explore herd-specific episodes using the default thresholds and compared results with the full data set.

RESULTS

Descriptive Analyses

We analyzed 2,584 episode sequences from 15 herds. Table 1 displays descriptive statistics per herd for cows according to our definition of udder inflammation. The herds varied greatly in terms of proportions of days with diverted milk, duration of milk diversion, mean daily milk yield, median day of initial inflammation, mean SCC, number of lactations, and number of observations. Figure 2 shows the progression of the fraction of cows <200,000 cells/mL per day for the 4 subsets after the start of the episode up to 90 d after the start of the episode. For example, the recovery fraction in Figure 2 at d 10 after the initial inflammation was 68% of the cows in the no diverted milk–recovery subset; that is, cows that had an SCC observation <200,000 cells/mL. As expected, in the nonrecovery subsets (no diverted milk–no recovery and diverted milk–no recovery), the fraction remained low because, per the subset definition given in Material and Methods, the cows in this subset did not have 10 consecutive days with a mean SCC <200,000 cells/mL. In both recovery subsets (no diverted milk–recovery and diverted milk–recovery), the fraction increased substantially during the first 20 to 30 d after the initial inflammation, up to 65 to 80% of the cows in the respective subsets. The recovery fraction of the no diverted milk–recovery subset increased substantially faster than its diverted milk–recovery counterpart. Extra descriptive analysis on general herd information and descriptive analysis per subset are presented in Appendix Tables A1 and A2.

Linear Mixed Model Analyses

Somatic Cell Count. Somatic cell count in the week of the initial inflammation (i.e., week since initial inflammation = 0) was significantly higher than in most other weeks in all subsets (Table 2). However, the subset no diverted milk–no recovery was different, because the mean SCC at the week of the initial inflammation was not significantly higher than the weeks after the week of the initial inflammation. The standard deviation of the cow lactation random effect was larger than the standard deviation of the herd random effect for all SCC subset models, indicating a larger variation in the residuals between cows than between herds.

Figure 3 shows the estimated marginal means of the SCC from 4 wk before the initial inflammation to 12 wk after the initial inflammation. At mean level, the diverted milk–recovery subset had >200,000 cells/mL (natural logarithm of 200 is 5.298) at approximately 1 wk past the initial inflammation whereas that of the no diverted milk–recovery subset was <200,000 cells/mL in the week of the initial inflammation. Moreover, SCC in both the diverted milk–recovery and no diverted milk–recovery subsets stabilized approximately 3 to 4 wk after the initial inflammation at a level slightly higher than that before the initial inflammation. As expected in the diverted milk–no recovery and no diverted milk–no recovery subsets, mean SCC remained stable and was, on average, >200,000 cells/mL after the initial inflammation throughout the 12-wk time window and higher compared with the level before initial inflammation. The average levels of SCC increased before the initial inflammation in all subsets except in the diverted milk–no recovery subset. Last, the average SCC value during the week of the initial inflammation of SCC of the diverted-milk subsets was higher than that of the no-diverted-milk subsets.

σ-Conductivity. Results from the multivariable analysis of σ-conductivity are presented in Table 2. σ-Conductivity in the week of initial inflammation was significantly different from that in most other weeks after the initial inflammation in all subsets, except for several weeks after initial inflammation in the no diverted milk–no recovery subset. However, even in the 3 other subsets, the difference in the later weeks was less substantial than in the SCC subsets due, in part, to an increase in standard errors of the weekly coefficients. The standard deviation of the cow lactation random effect was larger than that of the herd random effect for all subsets, indicating greater variation in the residuals between cows than between herds.

Table 1. Descriptive statistics of the variables under study in the data set of cows with an udder inflammation episode according to our definition of udder inflammation in the selected herds

Herd number	Mean milk diversion proportion[1]	Mean duration of consecutive milk diversion (d)	Mean milk yield (kg/d)	Median DIM of initial inflammation after 10 DIM	Mean σ-conductivity[2]	Mean SCC[3]	Mean days between OCC samples[3]	No. of lactations	No. of milking days
1	0.01	2.79	36.35	23	−1.84	4.58	1.39	152	15,717
2	0.01	6.34	36.56	18	−1.73	4.82	1.50	468	45,611
3	0.04	2.22	38.41	23	−1.74	4.73	2.28	225	22,632
4	0.04	6.10	48.31	13	−1.90	4.79	1.16	176	17,209
5	0.05	6.08	38.34	11	−1.90	4.63	1.33	126	11,878
6	0.06	2.55	35.65	12	−1.66	5.30	1.76	227	21,821
7	0.02	3.37	42.03	15	−1.89	4.80	2.06	450	44,364
8	0.08	3.14	42.72	11	−1.81	4.77	1.46	141	13,448
9	0.03	5.27	36.21	13	−1.92	4.38	1.25	84	8,198
10	0.01	4.72	32.68	23	−1.85	4.74	1.28	164	16,266
11	0.01	6.55	40.93	12	−1.87	4.72	1.59	89	8,337
12	0.04	4.21	34.06	13	−1.68	5.32	3.02	72	6,763
13	0.01	8.29	39.19	12	−2.01	4.02	1.32	98	9,403
14	0.02	6.79	35.49	27	−1.82	4.39	1.21	86	8,808
15	0.03	2.38	36.18	11	−1.82	4.81	1.48	26	2,428
Mean	0.03	4.72	38.21	15.80	−1.83	4.72	1.61	172.27	16,858.87
SD	0.02	1.92	3.98	5.49	0.09	0.32	0.50	129.04	12,698.72
Minimum	0.01	2.22	32.68	11	−2.01	4.02	1.16	26	2,428
Maximum	0.08	8.29	48.31	27	−1.66	5.32	3.02	468	45,611

[1]Diverted milk proportion = number of milkings with diversion/total number of observed milkings.

[2]σ-Conductivity = natural logarithm of the standard deviation between quarter conductivities as measured by the automatic milking system. It can be seen that σ-conductivity is negative as the natural logarithm of a value between 0 and 1 is negative.

[3]SCC = natural logarithm of the SCC as measured by Online Cell Counter (OCC; DeLaval International AB, Tumba, Sweden).

Figure 4 shows the estimated marginal means of σ-conductivity. As expected, the diverted milk–no recovery subset showed stable σ-conductivity values above the level after the initial inflammation, whereas the diverted milk–recovery subset stabilized in 3 to 4 wk after the initial inflammation, but above the estimated level before the initial inflammation. The no diverted milk–recovery and the no diverted milk–no recovery subsets did not show a clear increase in the week of initial inflammation and did not have a clear decrease after the week of initial inflammation. The average σ-conductivity increased before initial inflammation in all 4 subsets. The average σ-conductivity during the week of the initial inflammation of the diverted-milk subsets was higher than that of the no-diverted-milk subsets.

Overall. Somatic cell count and σ-conductivity had similar patterns in the estimated marginal means across subsets. However, in the recovery subsets, SCC stabilized relatively closer to the level before initial inflammation than σ-conductivity. Furthermore, σ-conductivity in the no milk diverted–recovery and the no milk diverted–no recovery subset had a less clear pattern than SCC. The residuals for the 4 subset models for both SCC and σ-conductivity were approximately normally distributed and homoscedastic, although the negative residuals at lower fitted values formed a pattern of diagonal lines in the fitted values residuals plot where no pattern should be present, possibly because of sensor measurement error. We estimate that this concerned approximately 1% of the milking-day observations, assuming that every measurement below ln(50) SCC with a standardized residual of −2 is subject to this measurement error.

In the sensitivity analysis, we applied different SCC thresholds to define initial inflammation and the recovery. We also applied different thresholds for milk diversion duration, the maximum number of days between the initial inflammation and milk diversion, and the maximum number of days between the initial inflammation and second SCC measurement ≥200,000 cells/mL. In the recovery definition, we changed the number of input days to compute the mean. Overall, the results of the sensitivity analysis remained similar to the original results. More specifically, changing the SCC threshold to 100,000 cells/mL (300,000 cells/mL) in the initial inflammation definition resulted in a slightly larger (similar) initial increase in recovery fraction after the initial inflammation. The estimated marginal means of SCC and σ-conductivity showed a slightly lower (higher) peak at wk 0. However, the duration until stabilization remained between 3 and 4 wk. When we changed the SCC threshold to 100,000 cells/mL (300,000 cells/mL) in our recovery definition, it resulted in a higher (similar) fraction of cows below 200,000 cells/mL in the recovery subgroups in the recovery fraction analysis. This change in our recovery definition also resulted in a slightly lower (higher) level at which SCC and σ-conductivity stabilized. However, the duration until stabilization remained between 3 and 4 wk in all plots. Changing the number of consecutive diversion days from 2 to 5 did not substantially change the recovery fraction or the estimated marginal means of SCC and σ-conductivity. We changed the maximum

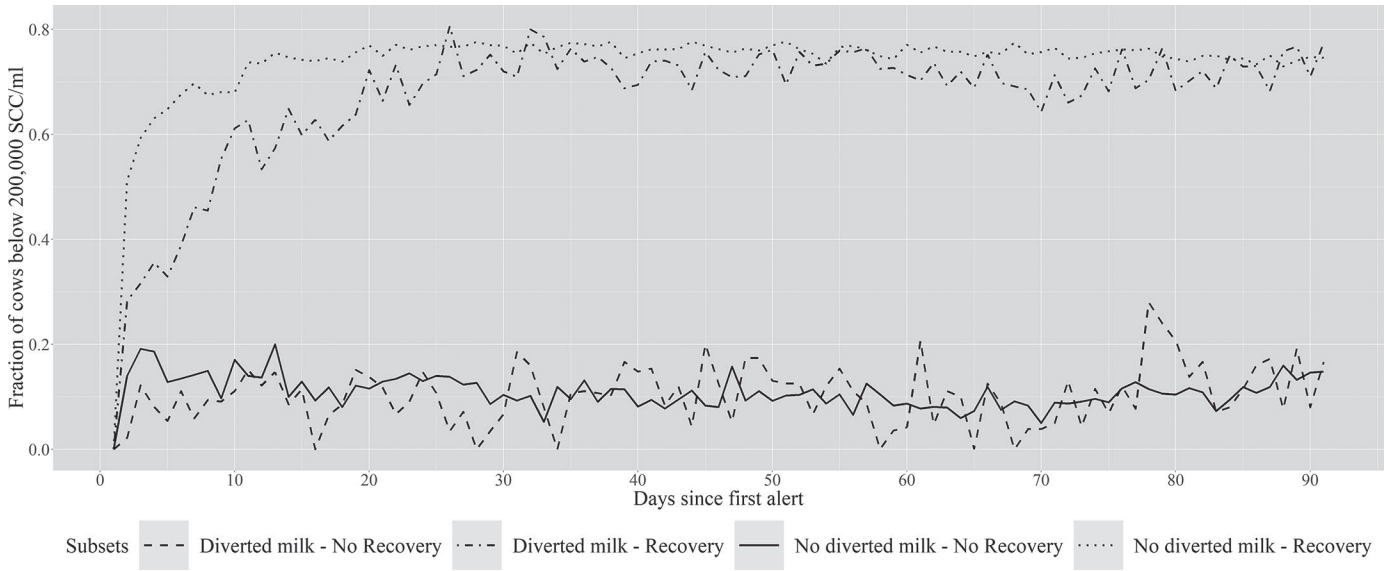

Figure 2. Progression of online SCC after initial inflammation (day = 0, first time in a lactation where SCC ≥200,000 cells/mL) in 4 subsets of cows as the fraction of cows with SCC <200,000 cells/mL relative to all cows in their respective subset from d 0 to 90.

Table 2. Estimated regression coefficients, standard deviation (SD) of the herd, cow, and residual random effects, first-order autocorrelation, and the number of herds, lactations, and observations from the SCC (cells/mL) and σ-conductivity models for 4 subsets of cows[1]

	SCC				σ-Conductivity			
	No recovery		Recovery		No recovery		Recovery	
Item	No diverted milk	Diverted milk	No diverted milk	Diverted milk	No diverted milk	Diverted milk	No diverted milk	Diverted milk
Week relative to first initial inflammation (SCC ≥200,000 cells/mL)								
−4	−2.209***	−2.438***	−1.213***	−2.403***	−0.292***	−0.833***	−0.132***	−0.993***
−3	−1.989***	−2.780***	−1.140***	−2.510***	−0.163***	−0.862***	−0.136***	−0.893***
−2	−1.890***	−2.754***	−1.117***	−2.273***	−0.146***	−0.795***	−0.097***	−0.825***
−1	−1.860***	−2.843***	−1.034***	−1.817***	−0.110***	−0.574***	−0.081***	−0.497***
0	−0.061	−0.341***	−0.415***	−0.615***	0.003	−0.164**	−0.016*	−0.144***
1	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
2	−0.020	−0.521***	−0.539***	−0.902***	0.010	−0.209**	−0.020*	−0.217***
3	−0.029	−0.506***	−0.598***	−1.029***	0.020	−0.166*	−0.032***	−0.225***
4	0.111*	−0.671***	−0.585***	−1.083***	0.029	−0.209*	−0.031**	−0.246***
5	0.181***	−0.657***	−0.563***	−1.014***	0.036	−0.207*	−0.026*	−0.230***
6	0.117*	−0.661***	−0.550***	−0.991***	0.039	−0.182†	−0.025*	−0.238***
7	0.117*	−0.694***	−0.540***	−0.979***	0.052†	−0.223†	−0.024†	−0.196*
8	0.213***	−0.695***	−0.519***	−0.947***	0.040	−0.219†	−0.035*	−0.183*
9	0.253***	−0.754***	−0.512***	−0.846***	0.075*	−0.149	−0.037*	−0.159
10	0.117*	−0.644**	−0.480***	−0.835***	0.005	−0.146	−0.035*	−0.109
11	0.127*	−1.059***	−0.444***	−0.730***	0.039	−0.142	−0.034†	−0.089
12	0.043	−0.909**	−0.419***	−0.717***	0.019	−0.222	−0.037*	−0.078
Other covariates								
DIM	−0.001*	0.004	−0.002***	−0.007**	0.001***	0.002	0.0001	−0.004**
Parity	0.145	0.439†	0.276***	0.566***	0.383***	0.495*	0.201***	0.434***
Constant	6.184***	6.379***	5.000***	5.682***	−1.750***	−1.527***	−1.994***	−1.540***
Random effect SD								
Herd	0.219	0.199	0.251	0.302	0.061	0.0004	0.102	0.045
Lactation	0.496	0.471	0.586	0.551	0.458	0.431	0.414	0.474
Residual	0.819	0.904	0.98	1.059	0.476	0.509	0.477	0.548
Residual AR(1)	0.377	0.35	0.300	0.466	0.447	0.432	0.385	0.504
Observations	14,240	2,617	133,290	11,037	23,766	3,876	184,140	14,430
Number of herds	15	11	15	15	15	11	15	15
Number of lactations	288	49	2,068	179	262	44	1,923	166

[1]Using the recovery definition and milk diversion status after the initial inflammation, the data set was split into 4 subsets of cows: (1) no diverted milk–no recovery, (2) diverted milk–no recovery, (3) no diverted milk–recovery, and (4) diverted milk–recovery.

†, *, **, and *** indicate significance of coefficient at $P = 0.1$, 0.05, 0.01, and 0.001, respectively, against the null hypothesis that the coefficient is equal to 0 and the alternative hypothesis that the coefficient is not equal to 0.

period between the initial inflammation and the second increased SCC observation equal to or higher than 200,000 cells/mL from 10 d to 5 and 20 d, which did not cause substantial differences in the estimated marginal means of SCC or σ-conductivity. However, the recovery fraction of the no diverted milk–recovery subset increased faster during the initial days after the initial inflammation but again plateaued after approximately 3 to 4 wk. Changing the maximum period between the initial inflammation and milk diversion from 10 d to 5 or 20 d did not substantially alter the recovery fraction results or the estimated marginal means of SCC or σ-conductivity. We changed the recovery period over which a SCC mean was computed, from 10 d to 5 and 20 d, which resulted in no substantial differences in the estimated marginal means of SCC or σ-conductivity, although the no-recovery subsets attained a higher recovery fraction when the recovery period was set to 5 d. Two herds with the largest number of selected episodes were also analyzed separately to explore herd-specific episode durations (data not shown). The confidence intervals of the weekly estimates increased substantially and it was hard to determine when the pattern would stabilize because of the limited number of observations. Taking this substantially increased uncertainty into account, we observed that the herd-specific episode durations until stabilization were approximately equal to 3 to 4 wk after the initial inflammation in both herds for SCC; that is, as found in the overall population. However, for the σ-conductivity analysis in 1 of the 2 individual herd data sets, we could not determine the same duration of 3 to 4 wk that we were able to determine in our main results. We observed no decrease of σ-conductivity after the initial inflammation and the confidence interval was very large.

DISCUSSION

In this study, we aimed to gain insight into the differences in udder inflammation indicators after an initial inflammation, as measured by AMS sensors, between cows that recover and cows that do not recover. Because this is one of the first studies to describe the duration of an udder inflammation episode based on

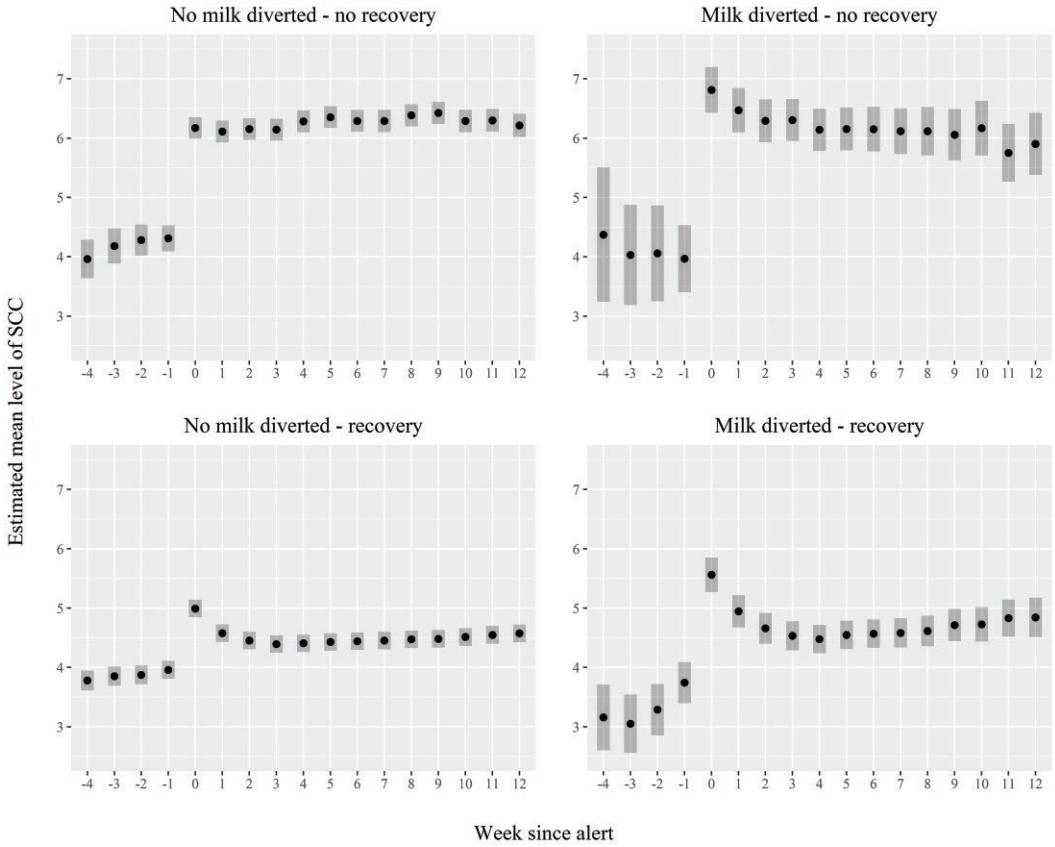

Figure 3. Patterns of SCC measured by online SCC from 4 wk before until 12 wk after the initial inflammation (first time in a lactation where SCC ≥200,000 cells/mL) for 4 subsets of cows using the estimated marginal effects of linear mixed models with 95% CI of the weekly mean.

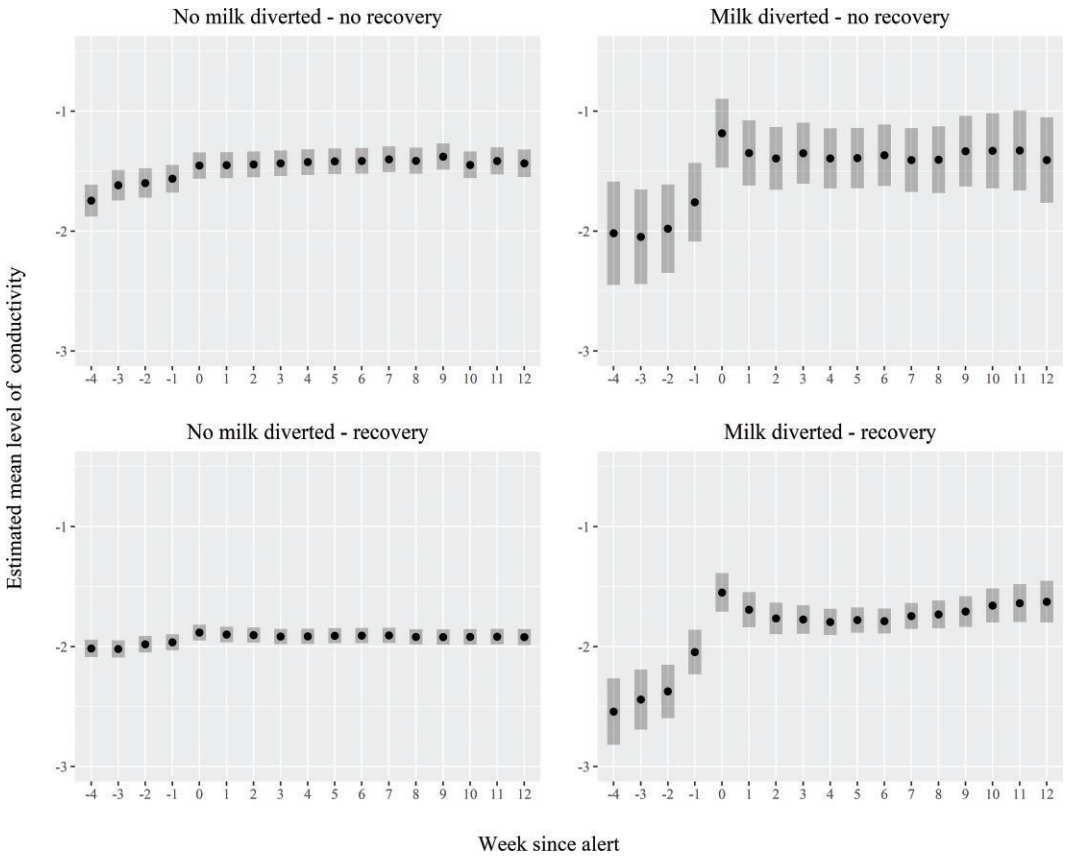

Figure 4. Patterns of σ-conductivity from 4 wk before until 12 wk after the initial inflammation (first time in a lactation where SCC ≥200,000 cells/mL) for 4 subsets of cows using the estimated marginal effects of linear mixed models with 95% CI of the weekly mean. It can be seen that σ-conductivity is negative because the natural logarithm of a value between 0 and 1 is negative.

daily sensor data, there was no standardized manner by which to define recovery or evaluate results. Our first major contribution is to show that it is possible to analyze the dynamics of inflammation indicators and gain insight into these dynamics using routinely available sensor and other data. Because farmers worldwide use similar sensors and management software, this creates interesting research and development opportunities as well as future practical applications. Second, our results showed that the mean of σ-conductivity and SCC stabilized, at most, 3 to 4 wk after the initial inflammation, above the level that occurred before the initial inflammation, depending on the inflammation indicator as SCC stabilized closer to the pre-onset level than did σ-conductivity. However, we also found that there was only a limited increase in σ-conductivity in both no-milk-diverted subsets. This could be due to the SCC-based case definition. Another case definition (that includes conductivity or a conductivity-based measure) would change the pattern in these subsets (data not shown). The observed recovery pattern would, in some cases, depend on the variables used in the case definition. It is important to consider that these are means, and substantial natural variation occurs in SCC and σ-conductivity; we observed a sizable residual variation compared with the size of the variation in residual herd- and cow-effects (Table 2). Nørstebø et al. (2019) argued that the normal variation of the SCC could cause high variability of OCC measurements. We observed that the estimated marginal mean value of σ-conductivity and SCC in the week of the initial inflammation was generally higher for diverted-milk subsets than for no-diverted-milk subsets. This most likely indicates a higher severity of the cases where farmers intervened by diverting the milk.

To date, no definitions of recovered and nonrecovered (i.e., chronic udder inflammation episodes) based on daily AMS measurements are available. Our findings showed distinctive mean patterns for both σ-conductivity and SCC during the course of an udder inflammation episode. Based on these mean SCC and σ-conductivity patterns, we suggest a cutoff point of 3 to 4 wk after initial inflammation to discriminate between chronic and recovered cases of udder inflam-

mation. Pinzón-Sánchez and Ruegg (2011) reported that 58.2% of the cows with clinical mastitis (which is different from our SCC-based case definition) returned to an SCC <200,000 cells/mL within 21 to 55 d after treatment based on DHI SCC, which is within the range of our findings. Somatic cell count and conductivity can be affected by factors other than mastitis. Harmon (1994) indicated that, aside from infection status, parity, stress, age, season, and stage of lactation can affect the variation in SCC. Other factors that may influence conductivity are temperature, stage of lactation, and milk composition (Nielen et al., 1992).

The use of sensors allowed us to study the dynamics of udder inflammation episodes on a large set of cows with daily measures; we analyzed 2,584 episodes almost daily for 90 d after the initial inflammation. In comparison, Francoz et al. (2017) mention 40 experimental treatment trials (out of 41 total trials summarized), studying treatments other than conventional antibiotics, that used a data sample consisting of, at most, 258 cows over, at most, 60 d after an onset of udder inflammation. Without sensor data, and other than carrying out expensive data collection schemes, the dynamics of mastitis could only be studied using DHI data, which has a bimonthly or monthly test frequency. A major disadvantage of using large observational data rather than smaller detailed observational or experimental data is that information on relevant factors may be missing. In our case, these would be data on bacteriology, clinical severity scores (if clinical signs were observed), or farmer criteria for initiating milk diversion and mastitis treatments as several other studies report (see Francoz et al., 2017, for examples). In terms of bacteriology, inflammation patterns can differ between different pathogens (Fogsgaard et al., 2015) or can be more associated with certain pathogens (de Haas et al., 2004) and could be used as the onset of an episode. Moreover, scoring the severity of clinical mastitis, if clinical mastitis was observed, could have given more insights into farmer decision-making and effects of mastitis severity on the progression and chances of recovery. Because farmer criteria for initiating treatments were not available, differences in farmer treatment decision-making (Espetvedt et al., 2013) could have influenced our results. However, the standard deviation in the random herd effect was low compared with that of the random cow lactation effect, indicating limited herd effects on average (e.g., due to a difference in treatment protocol) compared with the cow effect. Nonetheless, we could not completely control for the differences between herds, as we did not have access to the treatment protocols or background information on cases of the farms in our sample. Missing data on important factors is one inherent weakness of analyzing observational data retrospectively. Nevertheless, the extensive usage of observational data sets procured by DHI associations in research has led to insightful results on the general udder health status of herds as well as the association between milk production and SCC in the past (Tyler et al., 1989; Dohoo and Morris, 1993; Hand et al., 2012). Observational data sets can be used to describe general patterns. Therefore, we argue that large data sets with less detailed data can be used to explore and describe general patterns and associations in a larger population, and this type of observational study could be the first step to future research using more detailed but smaller data sets to study these general patterns in more detail.

Mean σ-conductivity stabilized above the level before initial inflammation, whereas mean SCC stabilized close to the level before initial inflammation. Furthermore, mean σ-conductivity showed a less substantial increase in the week of initial inflammation than SCC. Conductivity and SCC measures, as used in this study, are distinct udder inflammation indicators that are medium to highly correlated when transformed appropriately (Nielen et al., 1992). This is caused by both indicators measuring related but distinct processes associated with inflammation (Viguier et al., 2009); SCC in milk is largely the result of an activated immune response when PMN are released into the milk to engulf the pathogen. Then, apoptosis occurs and somatic cells can be found in the milk. Differences in conductivity occur through tissue damage and breaching of the blood–milk barrier. Tissue damage can also be caused by the PMN themselves as well as by the pathogen (Zhao and Lacasse, 2008). We hypothesize that the tissue damage remains even after an episode, causing a lasting weak point in the blood–milk barrier and affecting conductivity. Therefore, it can be expected that mean SCC and σ-conductivity would not share exactly the same pattern.

In this study, we focused on the progression of inflammation indicators after an initial inflammation and we assumed that SCC (measured by OCC) and standard deviation (σ) of conductivity are relevant to measure this progression. We did not aim to assess the diagnostic quality of SCC or conductivity, as this has already been studied (Nielen et al., 1992; Dalen et al., 2019); in addition, the diagnostic quality of OCC SCC was studied by Nørstebø et al. (2019) by comparing it with DHI SCC. They found a mean correlation of 0.82 between SCC measured by the OCC and SCC as measured in a DHI laboratory. Fadul-Pacheco et al. (2018) also reported a high mean correlation coefficient of 0.91, ranging from 0.84 to 0.98 between herds, for OCC measurements and SCC as measured in a DHI laboratory. Interestingly, there were differences in accu-

racy reported for 4 farms, but high agreement between SCC measured by OCC and SCC measured by a DHI laboratory remained. Given that SCC measurements by OCC have similar test performance as DHI SCC, frequent or even daily measurements enable detailed investigations of the onset and course of inflammation indicators compared with monthly or bimonthly DHI SCC measurements. In this study, we developed a specific conductivity measure, standard deviation (σ)-conductivity, which is similar to the variation of quarter conductivities measures as used by Anglart et al. (2020). The diagnostic quality of conductivity was discussed in the meta review of Nielen et al. (1992), in which raw conductivity and relative differences were compared across different studies using different gold standards (SCC-based, California Mastitis Test, Wisconsin Mastitis Test, and IMI). They found that measures using raw conductivity levels had a median specificity of 91% and median sensitivity 57%), whereas measures based on the difference in conductivity between quarters had a median specificity of 96% and median sensitivity of 79%). This supports the use of a conductivity measure that looks at differences between quarters. We chose the natural logarithm of the standard deviation of quarter conductivity specifically because it resulted in homoscedastic and normally distributed residuals in our statistical analyses.

Treatment with antibiotics can have a large effect on the udder inflammation recovery of a cow (Barkema et al., 2006). However, the data set used in this study did not contain detailed treatment records and milk diversions were used as a proxy for farmer intervention because farmers will divert milk when they find the milk unfavorable for sale or consumption. This could be to avoid a high bulk tank SCC, to avoid milk with antibiotic residues in the bulk tank, or milk diversion during an alternative treatment. Milk diversion is relatively untested and might not be as precise as farmer treatment records, which is one limitation of this study. This study is exploratory in nature, utilizing data from a very large number of cows, and we argue therefore that it is useful to use a novel, possibly less precise, but widely available variable in AMS data sets. The threshold was set to 2 consecutive days when milk was diverted within 10 d after the initial inflammation. A typical duration of milk diversions in relation to antibiotic treatment may vary between and within herds due to differences in required milk withdrawal times between different antibiotic drugs and treatment regimens. In an economic simulation study, Steeneveld et al. (2011) used a 5-d milk withdrawal time for the shortest antibiotic treatment course. Using 2 consecutive days of milk diversion rather than 5 consecutive days of milk diversion might be too strict, but it was used to ensure that no treated cases entered the no-diverted-milk subsets. Short milk diversion periods could represent cases in which farmers determined that the milk was not suitable for human consumption, but decided not to treat the animal with antibiotics based on the visual appearance or sensor data. Nevertheless, the milk diversion and initial inflammations were happening in approximately the same time window (Appendix Figure A1).

In our research, we made use of SCC to perform a first screening of a potential onset of an udder inflammation episode, which we required to be followed up by at least one more observation of SCC $\geq$200,000 cells/mL within 10 d of the initial inflammation. Confirmation of an IMI by the presence of an udder pathogen was not feasible in our study because the participating farmers did not regularly collect milk samples for bacteriology. Potentially different farmer thresholds for bacteriology would have resulted in a different frequency and timing of bacteriological testing and thus would have biased our results. Instead, we analyzed the udder inflammation indicators an AMS farmer, or any farmer using the OCC system, would monitor. From a practical point of view, a farmer wants to know how long a case typically takes from the first moment of detection, here by a sensor system, to a possible recovery of udder inflammation. Therefore, our results show the progression of udder inflammation indicators from the onset detected by the system until 90 d after the initial inflammation. Nevertheless, defining onsets of inflammation solely on robotic sensor data is a significant limitation in our study. Future studies with more refined definitions based on nonrobotic reference data such as farmer-confirmed clinical observations or identification of udder pathogens would be useful to add to the results of this study.

A set of thresholds was used on milk diversions, SCC, and number of days after the initial inflammation to define the episode using SCC and the number of consecutive days to determine recovery (Figure 1). The robustness of the results subject to the exact values for these thresholds was tested in a sensitivity analysis. The different set of thresholds did change the number of episodes that would be in each subset. However, our results were mostly robust to different thresholds.

The analysis as applied and the recovery definitions as defined focused on analyzing single episodes of udder inflammation. From the perspective of sensors, it can be hard to distinguish a new flare-up due to a new IMI from recurrent udder inflammation due to a remaining IMI. Therefore, we chose to focus on the first flare-up or episode. Nevertheless, when we changed the recovery duration threshold from 10 d with a mean <200,000 cells/mL to 20 d with a mean <200,000 cells/mL, which

can include the time for extra flare-ups, it did not affect the duration estimate.

During analysis, we encountered a data issue because the negative residuals at lower fitted values formed a pattern of diagonal lines in the fitted values residuals plot where no pattern should be present. A closer investigation indicated that these values would have an improbably low SCC value (e.g., 1,000 cells/mL), and we attribute this to measurement error of the sensor. This behavior of the OCC has been reported in the literature (Nørstebø et al., 2019). Nevertheless, OCC values are highly correlated with DHI SCC observations (Nørstebø et al., 2019) so they can be used as an adequate measurement. Overall, we argue that this had a limited effect due to the relatively small number of these observations compared with the total number of observations.

Practically, farmers could use the knowledge of the typical duration threshold of 3 to 4 wk from an initial inflammation to a healthy state as an indication of when to reevaluate the udder health status of the cow and effects of any interventions. When a cow persists with high SCC or σ-conductivity values for longer than 3 to 4 wk after the initial inflammation, recovery will most likely not occur, at least not within the studied time period of 12 wk after the initial inflammation. Further research is necessary to determine the course of chronic udder inflammation in cows that did not recover during the study period and appropriate follow-up intervention. However, the severity of clinical signs should always be the most important factor in the intervention decision because of animal welfare concerns and may justify recurrent treatment. In addition, IMI status and specific bacteriological information should always be used to determine the type of intervention.

The results of this study represent an important step toward understanding differences in SCC and conductivity from the start of an udder inflammation episode and over the course of 12 wk. By including herds from different geographic regions and countries, we covered a wide range of different management styles represented within AMS herds.

CONCLUSIONS

We identified differences and similarities in mean σ-conductivity and SCC after initial inflammation as defined using SCC. In subsets of cows that recovered, both mean σ-conductivity and SCC stabilized 3 to 4 wk, after the initial inflammation. Therefore, the time point of 3 to 4 wk after the initial inflammation may be regarded as a threshold to discriminate between nonchronic and chronic udder inflammation and to help farmers in their intervention decisions. Nevertheless, differences were observed between mean σ-conductivity and SCC. Duration of an udder inflammation episode and differences in temporal patterns between sensors after initial inflammations are affected by a large range of other cow, pathogen, and treatment factors and need more research. Generally, combining AMS data with milk diversion data seems to be a promising approach to analyze temporal patterns of udder inflammation and to explore differences between nonchronic and chronic udder inflammation.

ACKNOWLEDGMENTS

This research was funded by an Industry PhD program of the Swedish Government (ref. no. N2017/036895/SK) and DeLaval International AB (Tumba, Sweden). We especially thank Bohao Liao (DeLaval International AB) for his help in collecting the data. John Bonestroo and Ilka C. Klaas are employed by DeLaval International AB. Mariska van der Voort, Nils Fall, Ulf Emanuelson, and Henk Hogeveen have no conflicts of interest to report.

REFERENCES

Anglart, D., C. Hallén-Sandgren, U. Emanuelson, and L. Rönnegård. 2020. Comparison of methods for predicting cow composite somatic cell counts. J. Dairy Sci. 103:8433–8442. https://doi.org/10.3168/jds.2020-18320.

Barkema, H. W., Y. H. Schukken, and R. N. Zadoks. 2006. Invited review: The role of cow, pathogen, and treatment regimen in the therapeutic success of bovine *Staphylococcus aureus* mastitis. J. Dairy Sci. 89:1877–1895. https://doi.org/10.3168/jds.S0022-0302(06)72256-1.

Bonestroo, J. H., I. C. Klaas, M. Van der Voort, N. Fall, H. Hogeveen, and U. Emanuelson. 2020. Using milk diversion in automatic milking systems to estimate incidence of mastitis in the absence of treatment records. Page 168–169 in Proc. National Mastitis Counc. Mtg., Orlando, FL. National Mastitis Council, New Prague, MN.

Burvenich, C., M. J. Paape, A. W. Hill, A. J. Guidry, R. H. Miller, R. Heyneman, W. D. J. Kremer, and A. Brand. 1994. Role of the neutrophil leucocyte in the local and systemic reactions during experimentally induced E. coli mastitis in cows immediately after calving. Vet. Q. 16:45–50. https://doi.org/10.1080/01652176.1994.9694416.

Dalen, G., A. Rachah, H. Nørstebø, Y. H. Schukken, and O. Reksen. 2019. The detection of intramammary infections using online somatic cell counts. J. Dairy Sci. 102:5419–5429. https://doi.org/10.3168/jds.2018-15295.

de Haas, Y., R. F. Veerkamp, H. W. Barkema, Y. T. Gröhn, and Y. H. Schukken. 2004. Associations between pathogen-specific cases of clinical mastitis and somatic cell count patterns. J. Dairy Sci. 87:95–105. https://doi.org/10.3168/jds.S0022-0302(04)73146-X.

Dohoo, I. R., and K. E. Leslie. 1991. Evaluation of changes in somatic cell counts as indicators of new intramammary infections. Prev. Vet. Med. 10:225–237. https://doi.org/10.1016/0167-5877(91)90006-N.

Dohoo, I. R., and R. S. Morris. 1993. Somatic cell count patterns in Prince Edward Island dairy herds. Prev. Vet. Med. 15:53–65. https://doi.org/10.1016/0167-5877(93)90075-5.

Espetvedt, M., A.-K. Lind, C. Wolff, S. Rintakoski, A.-M. Virtala, and A. Lindberg. 2013. Nordic dairy farmers' threshold for contacting a veterinarian and consequences for disease recording: Mild clinical

mastitis as an example. Prev. Vet. Med. 108:114–124. https://doi.org/10.1016/j.prevetmed.2012.07.014.
Fadul-Pacheco, L., M. Séguin, R. Lacroix, M. Grisé, E. Vasseur, and D. Lefebvre. 2018. Characterization of milk composition and somatic cell count estimates from automatic milking systems sensors. Pages 53–63 in Proceedings of the ICAR Conference, Auckland, New Zealand.
Fogsgaard, K. K., P. Løvendahl, T. W. Bennedsgaard, and S. Østergaard. 2015. Changes in milk yield, lactate dehydrogenase, milking frequency, and interquarter yield ratio persist for up to 8 weeks after antibiotic treatment of mastitis. J. Dairy Sci. 98:7686–7698. https://doi.org/10.3168/jds.2014-9204.
Francoz, D., V. Wellemans, J. P. Dupré, J. P. Roy, F. Labelle, P. Lacasse, and S. Dufour. 2017. Invited review: A systematic review and qualitative analysis of treatments other than conventional antimicrobials for clinical mastitis in dairy cows. J. Dairy Sci. 100:7751–7770. https://doi.org/10.3168/jds.2016-12512.
Hand, K. J., A. Godkin, and D. F. Kelton. 2012. Milk production and somatic cell counts: a cow-level analysis. J. Dairy Sci. 95:1358–1362. https://doi.org/10.3168/jds.2011-4927.
Harmon, R. J. 1994. Physiology of mastitis and factors affecting somatic cell counts. J. Dairy Sci. 77:2103–2112. https://doi.org/10.3168/jds.S0022-0302(94)77153-8.
Hogeveen, H., C. Kamphuis, W. Steeneveld, and H. Mollenhorst. 2010. Sensors and clinical mastitis—The quest for the perfect alert. Sensors (Basel) 10:7991–8009. https://doi.org/10.3390/s100907991.
Hogeveen, H., W. Steeneveld, and C. A. Wolf. 2019. Production diseases reduce the efficiency of dairy production: A review of the results, methods, and approaches regarding the economics of mastitis. Annu. Rev. Resour. Econ. 11:289–312. https://doi.org/10.1146/annurev-resource-100518-093954.
Jones, G. M., R. E. Pearson, G. A. Clabaugh, and C. W. Heald. 1984. Relationships between somatic cell counts and milk production. J. Dairy Sci. 67:1823–1831. https://doi.org/10.3168/jds.S0022-0302(84)81510-6.
Kruze, J., A. Ceballos, H. Stryhn, A. Mella, R. Matamoros, P. A. Contreras, V. Leyan, and F. Wittwer. 2007. Somatic cell count in milk of selenium-supplemented dairy cows after an intramammary challenge with *Staphylococcus aureus*. J. Vet. Med. A Physiol. Pathol. Clin. Med. 54:478–483. https://doi.org/10.1111/j.1439-0442.2007.00999.x.
Milner, P., K. L. Page, and J. E. Hillerton. 1997. The effects of early antibiotic treatment following diagnosis of mastitis detected by a change in the electrical conductivity of milk. J. Dairy Sci. 80:859–863. https://doi.org/10.3168/jds.S0022-0302(97)76008-9.
Moyes, K. M., J. K. Drackley, J. L. Salak-Johnson, D. E. Morin, J. C. Hope, and J. J. Loor. 2009. Dietary-induced negative energy balance has minimal effects on innate immunity during a *Streptococcus uberis* mastitis challenge in dairy cows during midlactation. J. Dairy Sci. 92:4301–4316. https://doi.org/10.3168/jds.2009-2170.
Nielen, M., H. Deluyker, Y. H. Schukken, and A. Brand. 1992. Electrical conductivity of milk: measurement, modifiers, and meta analysis of mastitis detection performance. J. Dairy Sci. 75:606–614. https://doi.org/10.3168/jds.S0022-0302(92)77798-4.
Nørstebø, H., G. Dalen, A. Rachah, B. Heringstad, A. C. Whist, A. Nødtvedt, and O. Reksen. 2019. Factors associated with milking-to-milking variability in somatic cell counts from healthy cows in an automatic milking system. Prev. Vet. Med. 172:104786. https://doi.org/10.1016/j.prevetmed.2019.104786.
Pinheiro, J., D. Bates, S. DebRoy, D. Sarkar, and R Core Team. 2019. nlme: Linear and nonlinear mixed effects models. R package version 3.1–137. https://www.R-project.org/.
Pinzón-Sánchez, C., and P. L. Ruegg. 2011. Risk factors associated with short-term post-treatment outcomes of clinical mastitis. J. Dairy Sci. 94:3397–3410. https://doi.org/10.3168/jds.2010-3925.
Shuster, D. E., E. K. Lee, and J. M. E. Kehrli. 1996. Bacterial growth, inflammatory cytokine production, and neutrophil recruitment during coliform mastitis in cows within ten days after calving, compared with cows at midlactation. Am. J. Vet. Res. 57:1569–1575.
Smith, K. L., J. E. Hillerton, and R. J. Harmon. 2001. Guidelines on normal and abnormal raw milk based on somatic cell counts and signs of clinical mastitis. National Mastitis Council, Madison, WI.
Steeneveld, W., T. van Werven, H. W. Barkema, and H. Hogeveen. 2011. Cow-specific treatment of clinical mastitis: An economic approach. J. Dairy Sci. 94:174–188. https://doi.org/10.3168/jds.2010-3367.
St. Rose, S. G., J. M. Swinkels, W. D. J. Kremer, C. L. J. J. Kruitwagen, and R. N. Zadoks. 2003. Effect of penethamate hydriodide treatment on bacteriological cure, somatic cell count and milk production of cows and quarters with chronic subclinical *Streptococcus uberis* or *Streptococcus dysgalactiae* infection. J. Dairy Res. 70:387–394. https://doi.org/10.1017/S0022029903006460.
Tyler, J. W., M. C. Thurmond, and L. Lasslo. 1989. Relationship between test-day measures of somatic cell count and milk production in California dairy cows. Can. J. Vet. Res. 53:182–187.
Viguier, C., S. Arora, N. Gilmartin, K. Welbeck, and R. O'Kennedy. 2009. Mastitis detection: Current trends and future perspectives. Trends Biotechnol. 27:486–493. https://doi.org/10.1016/j.tibtech.2009.05.004.
Zhao, X., and P. Lacasse. 2008. Mammary tissue damage during bovine mastitis: Causes and control. J. Anim. Sci. 86(Suppl_13):57–65. https://doi.org/10.2527/jas.2007-0302.

ORCIDS

John Bonestroo https://orcid.org/0000-0001-8815-6357
Mariska van der Voort https://orcid.org/0000-0003-0503-259X
Nils Fall https://orcid.org/0000-0001-5597-2358
Henk Hogeveen https://orcid.org/0000-0002-9443-1412
Ulf Emanuelson https://orcid.org/0000-0001-7889-417X
Ilka Christine Klaas https://orcid.org/0000-0002-1397-8505

APPENDIX

Table A1. Descriptive statistics of the variables under study in the data set of both the selected cows with an udder inflammation episode according to our definition of an inflammation case and not-selected cows in the selected herds from January 4, 2016, to March 14, 2019

Herd no.	No. of milking days	Mean diverted milk fraction[1]	Mean milk yield (kg/d)	Mean SCC[2] ($\times 10^3$ cells/mL)	No. of OCC samples	No. of lactations	Mean days between OCC samples	Fraction of primiparous cows
1	98,162	0.01	31.90	184.05	60,326	469	1.63	0.32
2	442,836	0.01	30.84	225.56	242,438	2,121	1.83	0.39
3	159,131	0.03	34.26	188.07	54,328	673	2.93	0.34
4	112,357	0.02	39.85	216.58	83,666	491	1.34	0.28
5	72,465	0.03	32.27	209.22	53,937	376	1.34	0.33
6	130,334	0.05	29.37	333.46	54,012	519	2.41	0.37
7	222,373	0.03	37.38	234.58	85,733	1,323	2.59	0.43
8	88,503	0.05	36.97	210.23	58,050	500	1.52	0.42
9	51,891	0.02	30.14	203.89	38,692	224	1.34	0.42
10	111,233	0.01	30.18	261.84	39,360	440	2.83	0.23
11	59,894	0.01	32.75	174.88	36,513	277	1.64	0.29
12	62,423	0.01	29.61	371.76	9,758	307	6.40	0.29
13	57,207	0.01	32.45	142.02	42,231	289	1.35	0.26
14	57,549	0.01	30.82	134.08	30,076	273	1.91	0.34
15	12,876	0.05	28.84	277.93	9,254	138	1.39	0.35
Mean	115,948.93	0.02	32.51	224.54	59,891.60	561.33	2.16	0.34
SD	103,800.74	0.02	3.27	65.05	55,004.34	513.33	1.30	0.06
Minimum	12,876	0.01	28.84	134.08	9,254	138	1.34	0.23
Maximum	442,836	0.05	39.85	371.76	242,438	2,121	6.40	0.43

[1]Diverted milk fraction = number of diverted observations/total number of observations.

[2]SCC = SCC as measured by Online Cell Counter (OCC; DeLaval International AB, Tumba, Sweden).

Table A2. Descriptive statistics of the variables under study in the data set of the selected cows with an udder inflammation episode according to our definition of an inflammation case per subset

Subset	No. of milking days	Diverted milk fraction[1]	Mean milk yield (kg/d)	Mean SCC[2] ($\times 10^3$ cells/mL)	No. of OCC samples	No. of lactations	Average days between OCC samples	Fraction of primiparous cows
No diverted milk, no recovery	27,003	0.05	40.59	6.25	14,240	288	1.90	0.14
Diverted milk, no recovery	4,615	0.17	39.66	6.41	2,617	49	1.76	0.11
No diverted milk, recovery	204,344	0.02	38.47	4.54	133,290	2,068	1.53	0.35
Diverted milk, recovery	16,921	0.12	37.84	4.81	11,037	179	1.53	0.35

[1]Diverted milk fraction = number of diverted observations/total number of observations; no diverted milk subsets have a nonzero mean value because of milk diversions after the 10 d after the initial inflammation (first time in a lactation where SCC $\geq$200,000 cells/mL).

[2]SCC = SCC as measured by Online Cell Counter (OCC; DeLaval International AB, Tumba, Sweden).

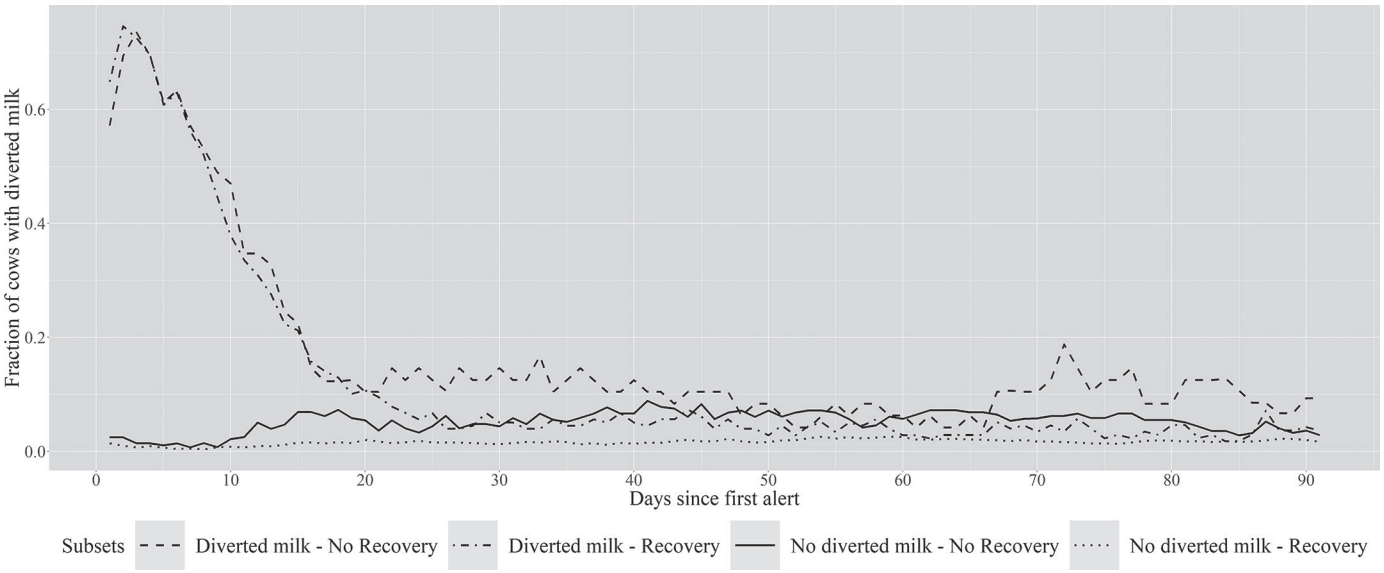

Figure A1. Progression of milk diversions after the initial inflammation (day = 0, first time in a lactation where SCC ≥200,000 cells/mL) in 4 subsets of cows from d 0 to 90. The figure shows the fraction of cows with diverted milk over all recorded cows in the recovery and no recovery subsets after the initial inflammation (first time in a lactation where SCC ≥200,000 cells/mL). In the recovery cases, milk diversions and recoveries were well aligned. This suggests that the farmer is also inclined to think that these cows are recovered and therefore the farmer allows their milk to be placed in the bulk tank again. In the nonrecovery case, the diverted milk fraction showed larger variation than in the recovered subset after 20 d after the initial inflammation. In these cases, the initial inflammation and the apparent intervention were less aligned than in the recovered cases. In the case of recovery as well as nonrecovery, a clear peak of diverted milk fraction could be seen in the first 20 d after the initial inflammation. This also makes sense as the sum of days of antibiotic treatments and the subsequent necessary period of milk diversion usually last between 5 and 10 d. Some interventions may have been started later, which could prolong the period of increased diverted milk fraction to 20 d.