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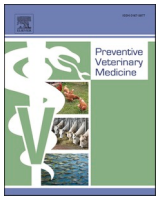

Dry cow therapy and early lactation udder health problems—Associations and risk factors

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ABSTRACT

Mastitis remains the most expensive disease of dairy cows, and antibiotic dry cow therapy (DCT) at dry-off is an important part of mastitis control. Regardless of the infection status, blanket DCT is administered to all quarters of all cows, which is controversial due to the worldwide problem of antimicrobial resistance. Even though selective DCT of only infected cows is a more sustainable approach, choosing animals for treatment is not always straightforward. Our aim was to evaluate whether the herd-level DCT approach is associated with early lactation udder health problems, taking into account the cow characteristics. The information source was 2015–2017 Dairy Herd Improvement data with 7461 multiparous cows from 241 Finnish dairy herds. Information on the herd-level DCT approach was obtained from farmers' questionnaire responses in 2017, and the three different approaches were selective DCT, blanket DCT, and no DCT. The statistical tool for the data analysis was a generalized linear mixed model with a random herd effect for binary outcomes and a linear mixed model with a random herd effect for a continuous outcome. The two binary outcomes were the odds of having high milk somatic cell count (SCC $\geq$ 200 000 cells/mL) on the first test-day within 5–45 days in milk (DIM) and the odds of mastitis treatment in early lactation up to 45 DIM. The third outcome was the mean milk lnSCC ($\times$ 1000 cells/mL) within 120 DIM. Selective DCT was the prevailing treatment practice in our data. Blanket DCT was associated with lower SCC after calving. Cows more likely to have high SCC after calving were older cows, cows with high average SCC during the previous lactation, and cows with high milk yield near dry-off. A mastitis treatment in the early lactation was more likely if, during the previous lactation, the cow had high average SCC, high peak milk production, or high milk yield near dry-off. Our findings indicate that DCT is still effective in mastitis control. Cows with high milk yield, especially near dry-off, and cows with persistently high SCC require attention when considering next lactation udder health.

1. Introduction

Antibiotic dry cow therapy (DCT) effectively reduces the prevalence of bacterial intramammary infections (IMI) in dairy cows (Dingwell et al., 2003; Bradley and Green, 2004). The susceptibility of cows to mastitis particularly during the dry period and the large economic impact of mastitis emphasize the importance of DCT (Bradley and Green, 2004; Halasa et al., 2007). The DCT is administered either as a blanket treatment of all quarters of all cows or as a selective treatment of only infected cows or quarters. The use of non-antibiotic internal or external teat sealants (ITS, ETS) either alone or concurrently with DCT is an additional preventive measure against IMI (Rabiee and Lean, 2013; Winder et al., 2019a). The basis for treating all cows at dry-off was established over five decades ago in the 5-point mastitis plan against contagious pathogens (Neave et al., 1969), and blanket DCT is still a widely used tool in mastitis control around the world. Nevertheless, the Nordic guidelines for mastitis therapy have always recommended selective DCT, use of narrow-spectrum antibiotics, and a microbiological diagnosis of infected quarters (Ekman and Østerås, 2003; Vilar et al., 2018; Rajala-Schultz et al., 2019).

Globally, environmental mastitis pathogens are the most common causes for mastitis in modern dairy herds, and instead of antibiotics, the emphasis is on other mastitis prevention measures (Klaas and Zadoks, 2018). Furthermore, given the increasingly serious problem of

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antimicrobial resistance, it is not surprising that the use of antibiotics in dairy farming is a topic of an active discussion (World Health Organization, 2014, 2015; European Commission, 2015; EMA and EFSA, 2017). Despite the concerns towards antibiotic use in animal production, studies on mastitis pathogens have not shown a clear rise in the prevalence of resistance (Saini et al., 2012; de Jong et al., 2018). However, we have only limited knowledge about the intramammary microbiome and the transfer of resistance features within animal microbiomes, which consist mostly of commensal bacteria (Pärnanen et al., 2018). Already the manufacturing process of drugs produces harmful levels of antibiotic emissions, and together with the use of antibiotics, this most likely increases the selection pressure for resistance (Levy and Marshall, 2004; Larsson et al., 2007; Perry and Wright, 2013; Surette and Wright, 2017). Therefore, unnecessary administration of antibiotics is unsustainable, and the optimization of use is important for controlling the antibiotic consumption and release of antibiotic residues (Laxminarayan et al., 2013; Pruden et al., 2013), as also emphasized by the One Health approach (McEwen and Collignon, 2018). Since antibiotic DCT products account for a large proportion of drugs used in mastitis control, the use and efficacy of DCT in modern dairy herds are worth re-examining (Pol and Ruegg, 2007; Scherpenzeel et al., 2014; Vanhoudt et al., 2018).

Cow composite milk somatic cell count (SCC) is an easily obtained numeric value from the Dairy Herd Improvement (DHI) test-day measurements. A composite milk SCC of a healthy udder is typically < 100 000 cell/mL (Sordillo et al., 1997). The widely used threshold for IMI detection is SCC $\geq$ 200 000 cell/mL, and cows with SCC above this threshold are more likely to have IMI (Dohoo and Leslie, 1991; Schepers et al., 1997; Djabri et al., 2002; Pantoja et al., 2009b). The reported sensitivity and specificity of the latter threshold range from 0.64 to 0.89 and from 0.66 to 0.90, respectively (McDermott et al., 1982; Dohoo and Leslie, 1991; Schepers et al., 1997; Pantoja et al., 2009b). Sensitivity and specificity vary mainly due to the pathogen involved, the number of infected quarters, the time of milk sampling, and the limitations in bacteriological examination of milk. Intramammary infections caused by minor pathogens typically elicit more moderate SCC responses than those caused by major pathogens (Barkema et al., 1999).

Since the most challenging question of selective DCT is how to find the cows to be treated, studies have utilized test-day SCC information to find out the selection criteria for infected cows (Torres et al., 2008; Rajala-Schultz et al., 2011; Vasquez et al., 2018; Rowe et al., 2020b). Additionally, studies have used test-day SCC information in the evaluation of the infection dynamics across the dry period (Cook et al., 2002; Pantoja et al., 2009b; Madouasse et al., 2010; Dufour and Dohoo, 2012; Lipkens et al., 2019a, b). However, as the long-term use of selective DCT is so far limited mainly to the Nordic countries, observational studies in commercial dairy herds that utilize DHI data to compare different DCT approaches are scarce (Vanhoudt et al., 2018; Niemi et al., 2020).

Using retrospective DHI data, our objective was to determine whether the herd-level DCT approach is associated with early lactation udder health problems while taking into account the effect of cow characteristics.

2. Materials and methods

2.1. DHI data

Our initial data included DHI information from 22 270 cows registered in 241 conventional dairy herds during 2015–2017. Farmers responded to an online questionnaire in 2017. The questionnaire was available to all dairy farmers who belonged to the Finnish dairy herd recording system (equivalent to DHI) in 2016. During that year, approximately 70 % of Finnish herds and 80 % of Finnish cows belonged to the system. The responding farms amounted to 715 out of approximately 5400. Vilar et al. (2018) reported the information from the questionnaire. The farms included in this study granted permission to use their DHI data for research, and the data source was the Finnish Milk Recording database (MTech Digital Solutions, Vantaa, Finland). Niemi et al. (2020) reported the detailed herd-level information of these farms from 2012 to 2016.

DHI data included cow-level information on test-day SCC and milk production. Although the test-day interval for milk production measurements was typically one month, the usual interval for SCC measurements was either one or two months. For a small proportion of cows, test-day measurements were available at a two-week interval. Furthermore, data included information on 305-d milk production, 305-d energy-corrected milk production (ECM305), days in milk on a test-day (DIM), breed, parity, dry period length and recording of mastitis treatments. Data comprised only two predominant dairy breeds in Finland, Finnish Ayrshire and Holstein, which at the time of the study accounted for approximately 98 % of the national dairy population.

Farmers in Finland do not have access to antibiotic drugs without a prescription from a veterinarian. Thus, mastitis treatments are either given by a veterinarian or initiated based on veterinary advice. These treatments are recorded into a central health-recording database. The treatment records during lactation are classified as clinical and subclinical mastitis, but do not contain information on the clinical symptoms of mastitis or the severity of the symptoms. Consequently, all records of mastitis treatments were taken into account and were defined as a mastitis treatment during lactation. Dry cow therapy has a separate code. In some farms, the mandatory individual dry-cow treatment records are only stored on the farm and are not transferred to the dairy herd recording system. As a result, DHI data lacked reliable data on individual dry-cow treatments.

2.2. Exclusion criteria

After the exclusion of primiparous cows ($n = 9047$) and cows without test-day SCC measures ($n = 1764$), the latest calving was selected for every cow. DHI information comprised the early lactation after the calving and the entire preceding lactation. Cows with a dry period < 30 days or > 90 days were excluded ($n = 1394$) because those lengths were not considered representative of a typical dry period. Approximately 4 % of the cows lacked information on the date of dry-off. Therefore, cows with test-day measures within 40 days before calving and missing dry-off date ($n = 48$) were excluded due to the likelihood of an unusually short dry-period. Conversely, cows without test-day measures within 120 days before calving and missing dry-off date ($n = 37$) were excluded due to the likelihood of an unusually long dry period. Cows without a test-day SCC within 45 days post calving ($n = 2046$) were excluded to ensure that the first SCC-measurement was not too far from calving. Cows with a test-day SCC within 5 days post calving ($n = 473$) were excluded, because the first SCC measurement was considered being too shortly after calving (Barkema et al., 1999). Subsequently to the exclusions, the cows numbered 7461, and the herds numbered 241.

2.3. Antibiotic DCT strategies

The data comprised information on the herd-level DCT approach based on farmers' questionnaire answers between January and May 2017 (Vilar et al., 2018). Duration of the DCT approach used by the farm without changing the selected approach was from 1 to 5 years in 51 farms and over 5 years in 190 farms (Niemi et al., 2020). The type of DCT approach was a compulsory question and the three DCT-treatment categories were selective DCT, blanket DCT, and no DCT. In order to minimize misclassification bias, dry-off dates of the cows were between November 2015 and December 2017. Based on the questionnaire information, 73.4 % (141/192) of the selective DCT farms treated only up to 25 % their cows with DCT, and only 9.4 % (18/192) of these farms treated more than half of their cows at dry-off (Niemi et al., 2020). At the time of the study, the three antibiotic dry cow products on the Finnish market contained benzylpenicillin 400 000 IU and framycetin 100 mg

(Umpimycin vet, Boehringer Ingelheim Vetmedica GmbH, Germany), cloxacillin 500 mg (Orbenin retard vet, Zoetis Finland Oy, Finland), and ampicillin 250 mg and cloxacillin 500 mg (Kloxerate retard, Norbrook Laboratories Limited, Ireland).

2.4. Management of missing values

The effect of missing values on data analysis was as follows. The mean SCC of the previous lactation was calculated from the test-day measurements, and it was based on a minimum of five and maximum of 27 measurements. This measure was available from 6825 cows on 239 herds. The peak milk production during 0–120 d in the previous lactation was sought among the test-day milk production measures. This measure was missing from one cow. The calculated mean SCC during the early lactation, 5–120 DIM, was based on a minimum of two and maximum of eight measurements. This measure was available from 6187 cows on 240 herds. Dry period length was available from 7211 cows on 240 herds.

2.5. The approximation of late lactation milk production

Because the last test-day with milk production measure ranged from 34 to 153 days prior to calving, the measurements were not directly comparable. Therefore, for the 7461 cows, late lactation milk production was approximated on the median of the last test-day with milk production measure. This median of the last test-day was 79 days before calving. The approximation method was the following. The last four test-day milk measurements during the previous lactation were included for every cow, and each cow had to have minimum of two milk measurements. For all milk measurements used, the DIM was greater than 120 to ensure that the values were on the decreasing phase of a typical lactation curve (Macciotta et al., 2005). Based on these measures, a linear regression was fit for every cow. Due to the notable variability in the test-day intervals and the slopes of these linear regressions, the mean slope was averaged from all slopes. This mean slope was -0.10 kg/day decline in milk production in the late lactation. The linear approximation of milk production on day 79 before calving was performed through the cow's own last milk measurement 34–153 days prior to calving. The slope of this linear approximation was the described average milk decline of our data. The tool for approximation was R version 4.0.0 (R Core Team, 2018) using R Studio Version 1.3.959 (RStudio Team, 2020).

2.6. Statistical analysis

The early lactation udder health was evaluated with three different statistical models. The outcome of the first model was the odds of having milk SCC $\geq$ 200 000 cells/mL on the first test-day 5–45 DIM (binary). The outcome of the second model was the odds of mastitis treatment within 45 DIM (binary). The outcome of the third model was the mean milk lnSCC ($\times$ 1000 cells/mL) during 5–120 DIM (continuous). Data exploration was conducted according to the protocol described by Zuur et al. (2010). The unconditional analyses of the main effects and the analyses of the first-order interactions were carried out between the explanatory variables and the outcome variables. The statistical model for the continuous outcome was a linear mixed model (LMM) with a random herd effect and for the binary outcomes a generalized linear mixed model (GLMM) with logit link function and a random herd effect. The likelihood ratio tests indicated that the random herd effect contributed significantly to a better model fit (p-value $<$ 0.0001).

Three explanatory variables represented the preceding lactation udder health. These variables were mean lnSCC ($\times$ 1000 cells/mL) of the lactation (continuous), SCC ($\times$ 1000 cells/mL) on the last test-day 0–60 d before dry-off (categorical with three levels: $<$ 100, 100–250, $>$ 250), and the number of mastitis treatments during the lactation (categorical with three levels: 0, 1, $\geq$ 2). Although the three variables were associated (p-value $<$ 0.01) with the outcomes in the unconditional analysis, the inter-association of the variables indicated noticeable collinearity. Therefore, only the mean lnSCC of the previous lactation was considered in the further analysis. This variable, unlike the others, described the udder health of the preceding lactation over a longer period.

The explanatory variables that represented the preceding lactation milk production were peak milk production during 0–120 DIM ($\times$ 5 kg/d, continuous), ECM305 ($\times$ 1000 kg, continuous), and approximated milk production 79 d before calving ($\times$ 5 kg/d, continuous). These variables were associated (p-value $<$ 0.05) with the outcome variables in the unconditional analyses. The correlation between the peak milk production and the ECM305 was high (Pearson's r = 0.84). The correlation between approximated milk production 79 d before calving and ECM305 was low (Pearson's r = 0.36), and the correlation between approximated milk production 79 d before calving and the peak milk production was negligible (Pearson's r = 0.21). Taking into account the correlations, the variables considered in the further analyses were approximated milk production 79 d before calving and the peak milk production during 0–120 DIM in the previous lactation.

Other explanatory variables were DCT approach of the farm (categorical with three levels: selective DCT, blanket DCT, no DCT), DIM ($\times$ 30 d) on the last milk production measurement at the end of lactation (continuous), parity at calving (categorical with three levels: 2, 3, $\geq$ 4), dry period length ($\times$ 30 d, continuous), and breed (categorical with two levels: Finnish Ayrshire, Holstein). The variables that were associated with all outcomes in the unconditional analyses were DCT approach (p-value $<$ 0.1) and parity (p-value $<$ 0.01). DIM on the last milk-measurement before dry-off was associated (p-value $<$ 0.2) with the odds of having SCC $\geq$ 200 000 cells/mL on the first test-day 5–45 DIM and the mean milk lnSCC ($\times$ 1000 cells/mL) during 5–120 DIM. Breed was associated (p-value $<$ 0.001) with the odds of mastitis treatment within 45 DIM and with the mean lnSCC ($\times$ 1000 cells/mL) during 5–120 DIM.

Explanatory variables that were associated with the outcome were introduced to the respective full model with the manual backward elimination model-building procedure to identify statistically significant explanatory variables (p-value $<$ 0.05) of the final models. The DCT approach was included in the models regardless of whether it was statistically significant or not, as it was the main explanatory variable. When the outcome was the odds of mastitis treatment within 45 DIM, parity was forced into the final model as a confounding variable for the relationship between peak milk production and the outcome, mastitis. The mastitis treatment between 0–45 d after calving (categorical with two levels: yes, no) was included in the final model, when the mean lnSCC during 5–120 DIM was the outcome. DIM at first SCC-measurement after calving (categorical with seven levels) was tested as an explanatory variable in the model for the odds of having milk SCC $\geq$ 200 000 cells/mL on the first test-day 5–45 DIM. This variable did not have any effect on the coefficients of other explanatory variables and was thus omitted from the final model.

Model validation indicated that all models complied with underlying assumptions. In order to measure the goodness-of-fit, marginal and conditional coefficients of determination were calculated for the models using methodology described by Nakagawa and Schielzeth (2013) and Nakagawa et al. (2017). The coefficients of determination represent the proportion of variance explained by fixed effects, and fixed and random effects together. For GLMMs fitted to the binomial distribution, the described methods are the theoretical method (assumes the observation-scale variance is constant, $\pi^2/3$) and the delta method (approximates the observation-scale variance based on the data) (Nakagawa et al., 2017). As a final step, 10 000 data sets were randomly simulated from the three final models separately to verify that the models complied with the observed data. The percentage of zeros was calculated for each simulated data sets from binomial GLMMs and were compared with the respective percentage of zeros in the observed binomial outcome variables. The comparison indicated that the models could cope with the number of zeros in the data. The density curves of

the simulated data sets from the LMM were compared with the density curve of the observed mean milk lnSCC (× 1000 cells/mL) to verify that the simulated data did not divert too much from observed data. Statistical analyses were done with R version 4.0.0 (R Core Team, 2018) using R Studio Version 1.3.959 (RStudio Team, 2020) with the package lme4 (Bates et al., 2015). The package ggplot2 (Wickham, 2016) was used to produce graphs. The packages MuMIn (Barton, 2020) and r2glmm (Jaeger, 2017) were used to calculate the marginal and conditional coefficients of determination.

3. Results

3.1. Descriptive results

Tables 1 and 2 present the descriptive statistics of the DHI data for the study farms and cows. Most of the cows, 74.4 % (5550/7461), were from selective DCT farms, followed by 20.6 % (1539/7461) of cows coming from blanket DCT farms, and 5.0 % (372/7461) from no DCT farms. Of the 241 farms, 192 (79.7 %) were selective DCT farms, 35 (14.5 %) were blanket DCT farms, and 14 (5.8 %) no DCT farms. The sample appeared representative of Finnish dairy farms, although the study farms had slightly larger number of cows, higher milk production and lower SCC than the average Finnish farms at that time (Table 1).

Two breeds divided 50.0 % Finnish Ayrshire and 50.0 % Holstein, and the breed distribution was parallel across the DCT-approach groups. The proportion of cows with at least one mastitis treatment during the previous lactation was 11.2 % (838/7461), and the proportion of mastitis-treated cows during first 45 DIM was 7.0 % (519/7461). The median test-day of the last SCC-measurement was 27 d before dry-off and thus slightly differed from the median test-day of the last milk-measurement, which was 17 d before dry-off and 79 d before calving. The median test-day of the first SCC-measurement after calving was 22 d. The overall proportion of all cows with SCC ≥ 200 000 cells/mL on the last SCC-measurement before dry-off and on the first SCC-measurement after calving was similar between groups except for no DCT group. Although the mean approximated late lactation milk production near dry-off was approximately 20 kg/d across the DCT groups, the late lactation milk production of cows varied substantially. Likewise, 305-day milk production, 305-day ECM, and peak milk production of the previous lactation varied noticeably, while the mean values were similar across the DCT groups (Table 2).

3.2. The odds of having SCC ≥ 200 000 cells/mL after calving

Table 3 presents the results of the final model for the odds of having SCC ≥ 200 000 cells/mL on the first test-day 5−45 DIM. The OR for blanket DCT approach compared with selective DCT approach was 0.69 (95 % CI 0.54– 0.88); $p = 0.003$. High mean SCC in the previous lactation increased the odds of high SCC after calving. Cows with high milk production near dry-off were more likely to have high SCC after calving, although peak milk production in the early previous lactation was not statistically significantly associated to the odds of having high SCC. Additionally, cows more likely to have high SCC after calving were older cows, and cows with a long previous lactation based on high DIM on the last test-day before dry-off. The theoretical-method marginal and conditional coefficients of determination showed that the proportion of variance in the model explained by the fixed effects was 8.9 % and the proportion of variance explained by the fixed and random effects together was 13.7 %. The respective proportions of variance for the delta-method marginal and conditional coefficients of determination were 5.4 % and 8.4 %.

3.3. The odds of mastitis treatment after calving

Table 4 shows the results of the final model for the odds of mastitis treatment within 45 DIM. The OR for blanket DCT approach compared with selective DCT approach was 0.67 (95 % CI 0.45–1.02); $p = 0.06$. Cows more likely to have a mastitis treatment in early lactation were cows with high mean SCC during the previous lactation, cows with a high milk yield near dry-off, and cows with a high peak milk yield in the previous lactation. The theoretical-method marginal and conditional coefficients of determination showed that the proportion of variance in the model explained by the fixed effects was 3.9 % and the proportion of variance explained by the fixed and random effects together was 16.3 %. The respective proportions of variance for the delta-method marginal and conditional coefficients of determination were 2.4 % and 10.0 %.

3.4. Mean SCC within 120 DIM

Table 5 presents the results of the final model for the mean SCC during 5–120 DIM. The prediction of early lactation mean lnSCC was lower if a cow was from a blanket DCT farm compared with a cow from a selective DCT farm. At SCC of 100 000 cells/mL this corresponds to a decrease of 20 000 cells/mL. The prediction of mean lnSCC was higher, if a cow had mastitis treatment within 45 DIM, had high mean SCC during the previous lactation, or if a cow was in her third, fourth or higher lactation. The peak milk production in the previous lactation was not statistically significantly associated with the mean lnSCC, but a high milk yield near dry-off was associated with a higher prediction of mean lnSCC in the first four months of the subsequent lactation. At SCC of 100 000 cells/mL this corresponds to an increase of 8000 cells/mL for every 5 kg increase in approximated milk production 79 d before calving. The

Table 1
Annual Dairy Herd Improvement (DHI) information presented from 241 conventional dairy herds in 2016 (Niemi et al., 2020).

	Selective DCT[a] ($n = 192$)			Blanket DCT ($n = 35$)			No DCT ($n = 14$)			National database[b]
	Mean (median)	Min	Max	Mean (median)	Min	Max	Mean (median)	Min	Max	Mean
Herd size	49.5 (37.6)	13	314.7	77.9 (62.4)	15.4	254.7	46.1 (30.4)	15.7	153.7	41.5
SCC[c] (x 1000 cell/mL)	160.7 (163.0)	36	336	162.9 (157.0)	49	316	155.8 (166.5)	82.0	260.0	178
Milk production[d] (kg/cow)	9693.9 (9664.5)	6693	12486	10091.4 (9944.0)	7797	11600	10094.1 (10083.0)	7788	12367	9542
Parity	2.5 (2.5)	1.7	4.3	2.4 (2.4)	1.8	3.4	2.2 (2.3)	1.8	2.8	2.4
Calving interval (d)	402.7 (399.5)	365	507	404.2 (402)	365	445	409.1 (410.5)	382	435	410
Milking system	Number (%)			Number (%)			Number (%)			
Pipeline	97 (50.5)			10 (28.6)			11 (78.6)			
AMS[e]	40 (20.8)			16 (45.7)			1 (7.1)			
Parlor	55 (28.7)			9 (25.7)			2 (14.3)			

[a] Dry cow therapy.
[b] Finnish Milk Recording System (2016).
[c] Somatic cell count. Annual herd-average of usually monthly or bimonthly milk SCC measurements of the individual cows.
[d] Annual herd-average of usually monthly milk production measurements of the individual cows.
[e] Automatic milking system.

Table 2
Dairy Herd Improvement (DHI) information from 7461 multiparous cows registered in 241 conventional dairy herds during 2015–2017.

	Selective DCT[a] (n = 5550)			Blanket DCT (n = 1539)			No DCT (n = 372)			All cows
	Mean (median)	Min	Max	Mean (median)	Min	Max	Mean (median)	Min	Max	Mean
Parity	3.3 (3)	2	11	3.1 (3)	2	10	3.1 (3)	2	8	3.3
Dry period length[b]	61.8 (61)	30	90	62.2 (61)	32	90	58.2 (57)	30	90	61.7
Mean test-day SCC (× 1000 cells/mL) of the previous lactation[c]	153.7 (75)	8.2	2915.8	157.8 (78.5)	9.8	4462	137.2 (78.6)	9.6	1650.4	153.7
Mean test-day SCC (× 1000 cells/mL) 5–120 d after calving[d]	227.8 (73.5)	4	8337.5	194.9 (51)	5.5	5950.5	216.5 (81.2)	6	2282.5	220.7
305-day milk production (kg) of the previous lactation[e]	9781.9 (9665.5)	3415	16931	10052.3 (10007)	3808	16701	9436.2 (9290.5)	3913	16324	9820.4
305-day ECM (kg) of the previous lactation[f]	10091.5 (10016)	2501	16852	10358.3 (10333)	4170	16561	9691.2 (9634)	3992	14163	10126.5
Peak milk production (kg/d) during 0–120 d in the previous lactation[g]	40.3 (39.8)	15.5	76.8	41.6 (41.4)	16.4	73.3	38.1 (37.2)	19.6	62.4	40.4
Approximated milk production (kg/d) 79 d before calving	20.4 (20.3)	1.6	48.0	21.3 (21.4)	3.1	40.9	21.2 (21.2)	4.3	47.5	20.6
Days in milk (DIM) on last test-day before dry-off	318.8 (307)	207	656	317.3 (305)	218	665	320.1 (308)	228	599	318.6
	Number (%)			Number (%)			Number (%)			Number (%)
SCC ≥ 200 000 cells/mL 0−60 d before dry-off[h]	1188 (23.3)			316 (22.8)			65 (19.5)			1569 (21.0)
SCC ≥ 200 000 cells/mL 5–45 d after calving	1347 (24.3)			292 (19.0)			101 (27.2)			1740 (23.3)
Mastitis treatment 0–45 d after calving	428 (7.7)			72 (4.7)			19 (5.1)			519 (7.0)

[a] Dry cow therapy.
[b] Number of missing values: 205 selective DCT, 39 blanket DCT, 6 no DCT, 250 all cows.
[c] Based on minimum of 5 and maximum of 27 test-day measures. Number of missing values: 407 selective DCT, 183 blanket DCT, 46 no DCT, 636 all cows.
[d] Somatic cell count. Based on minimum of 2 and maximum of 8 test-day measures. Number of missing values: 884 selective DCT, 300 blanket DCT, 90 no DCT, 1274 all cows.
[e] Number of missing values: 4 selective DCT, 2 blanket DCT, 6 all cows.
[f] Energy-corrected milk production. Number of missing values: 5 selective DCT, 2 blanket DCT, 7 all cows.
[g] Number of missing values: 1 no DCT.
[h] Number of missing test-day measures: 445 selective DCT, 152 blanket DCT, 39 no DCT, 636 all cows.

Table 3
Model estimates from logistic regression as a generalized linear mixed model for the odds of having milk somatic cell count (SCC) ≥ 200 000 cells/mL on the first test-day 5–45 days in milk (DIM), based on 6825 cows from 239 dairy herds.

Variable	Category	Coefficient	S.E.	z-value	p-value	OR	95 % CI	
Fixed effects								
Intercept		−4.55	0.27	−16.64	< 0.0001			
	No DCT	0.21	0.19	1.12	0.260	1.24	0.85	1.80
DCT[a] approach	Blanket DCT	−0.36	0.12	−2.91	0.003	0.69	0.54	0.88
	Selective DCT	Ref.						
Mean lnSCC (× 1000 cells/mL) of the previous lactation		0.44	0.02	14.97	< 0.0001	1.56	1.47	1.66
Approximated milk production 79 d before calving (× 5 kg/d)		0.10	0.02	4.45	< 0.0001	1.11	1.06	1.17
	≥ 4	0.41	0.07	5.59	< 0.0001	1.51	1.31	1.75
Parity	3	0.34	0.07	4.42	< 0.0001	1.41	1.21	1.64
	2	Ref.						
DIM on last test-day before dry-off (× 30 d)		0.05	0.01	3.13	0.001	1.05	1.02	1.09
Variable		Variance	S.D.					
Random effect								
Herd (Intercept)		0.184	0.429					

[a] Dry cow therapy.

marginal and conditional coefficients of determination showed that the proportion of variance in the model explained by the fixed effects was 12.9 % and the proportion of variance explained by the fixed and random effects together was 19.0 %. The proportion of variance explained by mean lnSCC of the previous lactation was 7.6 %, which was a considerably higher proportion compared to the other fixed effects of the model (Table 5).

4. Discussion

Recent herd-level results indicate that, although considerable variability exists among farms, the selective-DCT farms can reach long-term good udder health and milk production (Vanhoudt et al., 2018; Niemi et al., 2020). The previously reported differences in herd-level SCC and milk production among the DCT-approach groups were minor (Niemi et al., 2020), but the current cow-level results from the same farms showed that high SCC after calving was less likely, if a cow was a blanket-DCT farm cow compared with a selective-DCT farm cow. Although the use of DCT may have an effect on the odds of early lactation mastitis treatment, this study lacked statistical evidence to find differences between various DCT approaches. To the best of our knowledge, only one retrospective, observational cow-level selective

Table 4
Model estimates from logistic regression as a generalized linear mixed model for the odds of mastitis treatment within 45 days in milk (DIM), based on 6824 cows from 239 dairy herds.

Variable	Category	Coefficient	S.E.	z-value	*p*-value	OR	95 % CI	
Fixed effects								
Intercept		−5.15	0.36	−14.28	< 0.0001			
	No DCT	−0.39	0.35	−1.08	0.276	0.67	0.33	1.36
DCT[a] approach	Blanket DCT	−0.38	0.20	−1.85	0.063	0.67	0.45	1.02
	Selective DCT	Ref.						
Mean lnSCC[b] (× 1000 cells/mL) of the previous lactation		0.24	0.04	5.16	< 0.0001	1.28	1.16	1.40
Approximated milk production 79 d before calving (× 5 kg/d)		0.08	0.04	2.08	0.036	1.08	1.00	1.18
	≥ 4	−0.27	0.17	−1.62	0.104	0.75	0.54	1.05
Parity	3	−0.03	0.15	−0.19	0.844	0.97	0.71	1.31
	2	Ref.						
Peak milk production during 0–120 d in the previous lactation (× 5 kg/d)		0.13	0.04	3.18	0.001	1.13	1.05	1.23
Variable		Variance	S.D.					
Random effect								
Herd (Intercept)		0.487	0.698					

[a] Dry cow therapy.
[b] Somatic cell count.

Table 5
Model estimates from linear mixed model for the mean somatic cell count (lnSCC × 1000 cells/mL) during 5–120 days in milk (DIM), based on 5695 cows from 239 dairy herds.

Variable	Category	Coefficient	S.E.	t-value	*p*-value	$R^2_{GLMM(m)}$[a]	95 % CI	
Fixed effects								
Intercept		2.21	0.09	22.20	< 0.0001			
	No DCT	0.18	0.13	1.40	0.174	0.1	0	0.3
DCT[b] approach	Blanket DCT	−0.23	0.08	−2.91	0.002	0.5	0.2	0.9
	Selective DCT	Ref.						
Mean lnSCC (× 1000 cells/mL) of the previous lactation		0.36	0.01	21.49	< 0.0001	7.6	6.3	8.9
Approximated milk production 79 d before calving (× 5 kg/d)		0.08	0.01	6.21	< 0.0001	0.7	0.4	1.3
	≥ 4	0.31	0.04	7.64	< 0.0001	1.0	0.5	1.6
Parity	3	0.18	0.04	4.54	< 0.0001	0.3	0.1	0.7
	2	Ref.						
Mastitis treatment within 45 d after calving	Yes	0.58	0.06	9.43	< 0.0001	1.5	0.9	2.2
	No	Ref.						
Variable		Variance	S.D.					
Random effect								
Herd (Intercept)		0.113	0.336					
Residual		1.512	1.229					

[a] The proportion of variance (%) explained by the fixed effects (Nakagawa and Schielzeth, 2013).
[b] Dry cow therapy.

DCT-usage study exists prior the current study. In agreement with our results, that study showed higher odds of low SCC at the first test-day post-calving when antibiotic DCT was administered with or without ITS to the cow at dry-off (Vanhoudt et al., 2018). The main limitation of our study is that, instead of individual cow-level DCT treatment information, our study reports only herd-level information about the DCT treatments. Although the proportion of treated cows varies in selective DCT farms, the majority of the selective-DCT farmers of the current study reported treating only up to one fourth of their cows at dry-off. These proportions of treated cows were moderate and parallel to what has been reported before from the Nordic countries (Ekman and Østerås, 2003). In the Netherlands, selective DCT has been the national practice only since 2012 and the reported proportions of treated cows were higher (Scherpenzeel et al., 2016b; Vanhoudt et al., 2018). Economically, the optimum proportion of treated cows varies among farms, and the assessment and advice on cows in need of antibiotic DCT should be herd-specific (Huijps and Hogeveen, 2007; Halasa et al., 2010; Rajala-Schultz et al., 2011; Scherpenzeel et al., 2016a; Gussmann et al., 2018a; Scherpenzeel et al., 2018).

Our findings suggest that DCT remains an effective mastitis control tool in modern dairy farms. In agreement, the recent meta-analysis compared the efficacy of selective DCT versus blanket DCT and stated that risk of IMI at calving was higher in selectively treated cows, but considerable heterogeneity indicated more between-study variation than would be expected by chance (Winder et al., 2019b). The findings align with previous meta-analyses (Robert et al., 2006; Halasa et al., 2009). On the contrary, several experimental field studies with different study designs have reported that selective DCT had little or no negative effect on udder health and milk production on herd level (Bradley et al., 2010; Rajala-Schultz et al., 2011; Cameron et al., 2014, 2015; Vasquez et al., 2018), but opposite findings also exist (Berry and Hillerton, 2002a; McDougall, 2010; Scherpenzeel et al., 2014). The most recent studies combined selective DCT with concurrent ITS use, and the results consistently indicate that selective DCT has no negative effects on udder health (McParland et al., 2019; Rowe et al., 2020a, b). Compared with blanket DCT, the beneficial effect of selective DCT on the amount of antibiotics used is considerable and should not be overlooked (Pol and Ruegg, 2007; Scherpenzeel et al., 2014; Vanhoudt et al., 2018; Vasquez et al., 2018; McParland et al., 2019; Rowe et al., 2020a). Overall, DCT still appears to be an effective and useful tool in the management of udder health, but sufficient justification seems to lack for its prophylactic use in healthy animals. From the practical point of view, the puzzling question concerns the selection of cows to be treated at dry-off considering udder health, economics, antimicrobial resistance, and

sustainability concerns. Preferably, the treatment decision of the cow is based on longer-term udder health information, and ideally, microbiological analyses of presumably infected quarters is combined to the information before the decision (Østerås et al., 1999; Torres et al., 2008; Cameron et al., 2014; Vasquez et al., 2018).

The selective-DCT farmers of the current study took frequent microbiological milk samples at dry-off (Vilar et al., 2018; Niemi et al., 2020), which suggests that they often selected the animals for treatment based on the results of microbiological samples. The Finnish legislation requires that the antibiotic treatment decision and the choice of medicine are based on regular and adequate microbiological analyses (Finnish Ministry of Agriculture and Forestry regulation, 2014). Antibiotics for dairy farms are available in Finland merely with a veterinary prescription, and veterinarians do not have the right to profit from the sale of drugs. Thus, the proportion of treated cows in a herd is a joint decision of the farmer and the veterinarian. An indication for the use of blanket DCT is likely high prevalence of mastitis caused by contagious pathogens in a herd. Correspondingly, the most commonly reported reason for the no-DCT approach was good udder health (Vilar et al., 2018), which is supported by the low average herd-level SCC of this group (Table 1). Finnish recommendations are briefly as follows: 1) to delay the treatment of subclinical mastitis until dry-off, 2) to administer DCT to cows with a high SCC, especially during the last three months of lactation, based on either DHI measurements or data from automatic milking system, and 3) to administer DCT to cows treated for mastitis during preceding lactation. In addition, several cow- and pathogen-specific advice complement these recommendations and emphasize the need for microbiological milk samples. Although analysis of milk samples from all cows in a herd is not feasible economically or time-wise, regular and comprehensive microbiological milk sampling provides essential information on the known causal pathogens in the herd (Gussmann et al., 2018b; Ruegg, 2018). By combining information about a known pathogen with the onset of infection in relation to the lactation stage and the season, the infection pathways can be identified, and information on appropriate and effective mastitis prevention measures in a given herd can be considerably increased.

Susceptible, recurrently infected cows and chronically infected cows are likely to continue having udder health problems after dry period as the current results indicate that the cows with a higher long-term SCC are more likely to be treated for mastitis and have a higher SCC in the subsequent lactation. Moreover, the mean SCC of the previous lactation explained most of the variance in the mean SCC after calving compared with the other fixed effects. Previous studies support our observations. Lipkens et al. (2019b) reported that the lowest test-day SCC throughout the next lactation was observed in cows that had a test-day SCC $<$ 200 000 cell/mL both before and after dry-off. Several studies showed an association of higher late-lactation test-day SCC either with increasing test-day SCC or increasing likelihood of clinical mastitis in the subsequent lactation (Green et al., 2007; Whist and Østerås, 2007; Green et al., 2008; Gott et al., 2017; Vanhoudt et al., 2018). The current study noticed obvious collinearity between the explanatory variables of the preceding lactation udder health, which were mean test-day SCC, last test-day SCC, and number of mastitis treatments. Therefore, two out of three variables were omitted from the final models. However, all of these variables, or combinations of these variables, might be associated with the subsequent lactation udder health although their associations cannot be assessed simultaneously in the analyses of the current study. Susceptibility to recurrent mastitis exists also in quarter-level studies. The odds of clinical mastitis were 4.2 times higher in quarters that had a clinical mastitis during previous lactation compared with quarters without clinical mastitis (Pantoja et al., 2009a). Acquiring new infections during the dry period was more common in cows with a quarter already infected at dry-off (Neave et al., 1950; Rindsig et al., 1978; Berry and Hillerton, 2002b), and regardless of DCT, quarters infected at dry-off had higher odds of having IMI also at calving (Newman et al., 2010). Persistently infected quarters across the dry period had higher odds of clinical mastitis in early lactation compared to healthy quarters (Green et al., 2002; Pantoja et al., 2009a), and the occurrence of clinical mastitis in early lactation could indicate a mastitis problem that originated from the dry period (Green et al., 2002). The findings consistently emphasize the importance of mastitis prevention in the management of udder health, as a cow with a healthy udder is more likely to remain healthy in the future.

Despite a few studies reporting that higher milk yield at dry-off was not associated with higher post calving IMI proportion (Natzke et al., 1975; Gott et al., 2016), a number of studies have shown that IMI shortly after calving is more common in cows producing more milk at the point of dry-off (Oliver et al., 1956; Dingwell et al., 2004; Rajala-Schultz et al., 2005; Odensten et al., 2007; Newman et al., 2010). The association between the late lactation milk production with udder health of the subsequent early lactation, however, is a less-studied issue (Green et al., 2007, 2008; Madouasse et al., 2012; Gott et al., 2017). In agreement with our results, previous studies reported that higher milk production at the test-day within 0–30 d before dry-off was associated with an increased SCC after calving (Green et al., 2008; Madouasse et al., 2012; Gott et al., 2017). Our results showed that milk production at the end of lactation was associated with SCC even up to 120 d after calving, as has been reported before (Gott et al., 2017). Thus, the results suggest that late lactation milk production may have a long-standing influence on the early lactation udder health, but an opposite finding also exists. Odensten et al. (2007) stated that although milk production at the point of dry-off did influence IMI prevalence in the first week after calving, it did not influence SCC during the first month after calving. Interestingly, the current study found that the high milk production both in the preceding early and late lactation increased the odds of mastitis treatment in the subsequent early lactation. Quite the opposite, Green et al. (2007) found that neither 305-d yield nor the milk production at the last test-day prior to dry-off influenced the rate of clinical mastitis for a cow. Overall, the number of studies supporting that milk production near dry-off, or at the point of dry-off, influences the post-parturition udder health is more abundant than the number of studies that show otherwise. The frequently used explanations are that high-yielding cows may have incomplete teat-canal closure (Dingwell et al., 2004) and increased tendency to leak milk (Schukken et al., 1993; Tucker et al., 2009). Differences exist among the studies and results, which is probably due to dissimilarity in IMI definitions, study populations, and study designs. What is difficult to deduce, is the optimal amount of milk at dry-off and the feasible guidance for the farmers. In the majority of previous studies, cows received routine blanket DCT at dry-off. To the best of our knowledge, this is the first DHI data analysis of the effects of different DCT use in herds combined with the information about the milk production near dry-off. Worth mentioning is that almost all Finnish farms use gradual milk cessation method, and the milk yield of high-yielding cows decreases from the last test-day to the point of dry-off, being typically 15 kg/d or less (Vilar et al., 2018). Nevertheless, the current results showed that higher milk production at the end lactation, instead of high peak milk production at the early lactation, was associated with the higher post-parturition SCC.

An older cow is more likely to have mastitis (Dohoo et al., 1981), and SCC increases slightly with parity also in uninfected cows (Natzke et al., 1972). The association is reported repeatedly in numerous studies (Dingwell et al., 2004; Whist et al., 2006; Green et al., 2007, 2008; Pantoja et al., 2009a). In agreement, the current results showed that both the increased odds of having SCC $>$ 200 000 cells / ml at the first test-day and the higher mean SCC in early lactation were associated with higher parity. Regarding the odds of mastitis treatment, the parity was only a confounder for the relationship between peak milk production and mastitis. Pantoja et al. (2009a) reported that quarters of cows of greater than fourth parity were over four times more likely to have a case of clinical mastitis within 120 d after calving than quarters of cows of second parity, and higher parity is a potential risk factor for new dry period infections (Dingwell et al., 2004).

The Holstein breed has been more susceptible to both subclinical and clinical mastitis in previous studies (Persson Waller et al., 2009; Heikkilä et al., 2012; Hiitiö et al., 2017). Interestingly, the current study did not find enough statistical evidence to state that the Holstein breed was negatively associated with the early lactation udder health problems compared to Finnish Ayrshire breed. Noticeable inter-association was lacking between the breed and other variables, and thus the result was not due to the collinearity.

5. Conclusions

Cows more likely to have high SCC after calving were older cows, cows with high average SCC during the previous lactation, and cows with high milk yield near dry-off. Selective DCT was the prevailing treatment practice in our data. Blanket DCT was associated with lower SCC after calving. A mastitis treatment in the early lactation was more likely if, during the previous lactation, the cow had high average SCC, high peak milk production, or high milk yield near dry-off. Our findings indicate that DCT is still effective in mastitis control, however, in the light of antimicrobial resistance, it should be practiced in a selective manner. Cows with high milk yield, especially near dry-off, and cows with persistently high SCC require attention when considering next lactation udder health.

Declaration of Competing Interest

None.

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