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Randomized controlled field trial comparing quarter and cow level selective dry cow treatment using the California Mastitis Test

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ABSTRACT

Selective use of antibiotic dry cow treatment can be implemented at the cow or quarter level, with the latter having the potential to further reduce antibiotic use. Our objective was to compare these 2 approaches in 6 herds in the United Kingdom in which environmental mastitis predominated. Eight hundred seven cows were enrolled and categorized as having a high cell count (n = 401) or low cell count (n = 406) in the last 3 mo of lactation and clinical mastitis history. All quarters of all enrolled cows received an internal teat sealant. Within each category, cows were randomly allocated to 1 of 3 groups; in one group antibiotic treatment was allocated at cow level (i.e., all 4 quarters received antibiotic), whereas in the 2 remaining groups antibiotic treatment was allocated at quarter level, based on California Mastitis Test (CMT) findings. Two different thresholds, score 1 and 2, were used to determine likely infection status. Quarter milk samples were collected at dry off and postcalving for bacteriological culture and somatic cell count (SCC). Cows were monitored for clinical mastitis from dry off until 100 d in milk. Cow level SCC and milk yield data were collated from farm records. Within each category, the 2 quarter level treatment groups were compared with cow level treatment at dry off. Leaving quarters untreated with intramammary antibiotic in cows in the high cell count group, with a CMT <2 or <1, reduced antibiotic use by 55% and 31%, respectively, and resulted in no difference in the odds of being infected with any pathogen postcalving, but was associated with a higher SCC at the first test day. Intramammary antibiotic treatment of quarters with a CMT ≥1 in cows in the low cell count category at dry off was not associated with any reduction in the odds of being infected with a major pathogen postcalving but was associated with a decrease in the odds of being infected with a minor mastitis pathogen postcalving. The use of antibiotics in quarters of cows categorized as low cell count at dry off, increased the proportion of quarters treated with antibiotic from 0% at cow level to 31% (CMT ≥ 1) and 12% (CMT ≥ 2) at quarter level, only resulting in a reduction in SCC of around 20,000 cells/mL at the first test day, if all quarters with CMT score ≥1 were treated with antibiotic. No differences in clinical mastitis incidence and milk yield in the first 100 d in milk were detected between any of the treatment groups. These study findings support selective quarter level dry off treatment only in cows with cow level SCC >200,000 cells/mL at dry off.
Key words: selective dry cow treatment, California Mastitis Test, intramammary infection, antibiotic, teat sealant

INTRODUCTION

Antibiotic dry cow treatment is widely used for the cure and prevention of IMI (Halasa et al., 2009a,b). Three strategies have been recommended (Kabera et al., 2020; Rowe et al., 2020a): treatment of all cows to be dried off with antibiotics (**AB**) regardless of infection status (blanket cow level treatment, **BCLT**), treatment of all 4 quarters of infected cows (selective cow level treatment, **SCLT**), and treatment of infected quarters (selective quarter level treatment, **SQLT**).

Blanket cow level treatment has been a cornerstone of the "5-point plan" (Neave et al., 1969) for mastitis control for many decades, and has contributed to a significant reduction in IMI (Bradley, 2002). This reduction has, over time, resulted in AB at drying off (**DO**) being mainly prescribed in healthy, low SCC quarters to prevent new infections rather than for treating pre-existing infection. Increased public health concern about the prophylactic use of AB (European Medicines Agency, 2016), and the introduction of teat sealants as effective alternatives to prevent new infections, paved the way for SCLT.

Selective cow level treatment is well supported in the scientific literature (Green et al., 2002; Bradley et al., 2003; Scherpenzeel et al., 2014; Rowe et al., 2020a,b)

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and is increasingly implemented in dairy herds. Selective cow level treatment protocols are designed to use AB only in infected cows at DO. In the absence of alternative strategies for preventing new infection, such as an internal teat sealant, this approach leads to an increase in the risk for new IMI (Schukken et al., 1993; Berry and Hillerton, 2002a; Scherpenzeel et al., 2014). Internal teat sealants have been shown to be an effective alternative to AB for preventing new IMI in low SCC cows (Berry and Hillerton, 2002b; Huxley et al., 2002; Rabiee and Lean, 2013). However, a teat sealant is also recommended in infected cows combined with an AB treatment because combination treatment is equally (Vanhoudt et al., 2018; Kabera et al., 2020) or more effective (Newton et al., 2008; Bradley et al., 2010; Golder et al., 2016) in the prevention of new IMI, than AB alone. Therefore, SCLT programs increasingly advocate using a teat seal in all, both infected and uninfected, cows at DO.

Selective cow level treatment is performed at cow level because quarters have been considered interdependent within cows (Berry et al., 2003; Robert et al., 2006; Blagitz et al., 2015) and an increased risk of infection is perceived in uninfected quarters in infected cows. However, quarter interdependence may be less marked with environmental than contagious mastitis pathogens (Barkema et al., 1997) because the risk of new infection from the environment is assumed to be the same for all 4 quarters.

Selective quarter level treatment has been recommended some time ago (Osterås and Sandvik, 1996) and may indeed potentially be a more refined method of reducing the use of AB and result in equal overall dry period outcomes, when compared with SCLT (Patel et al., 2017). However, to date, SQLT is not well understood because peer-reviewed data on the outcome of dry period treatments allocated at quarter level are limited. In an Australian study (Browning et al., 1990), new infections were increased following quarter level treatment of cows infected at DO, though most infections were caused by *Streptococcus uberis* and *Staphylococcus aureus*. These findings, and those of Browning et al. (1994), may not be transferable to modern, well-managed herds with a low prevalence of contagious pathogens, and a mastitis etiology dominated by environmental pathogens such as *Escherichia coli*, other *Enterobacteriaceae*, and minor pathogens such as CNS and *Corynebacterium* spp., an etiology frequently seen in the United Kingdom. In herds with a low bulk milk somatic cell count (**BMSCC**) consistently <250,000 cells/mL for at least 12 mo, SQLT was shown to be a viable option to decrease antibiotic use by 58% without any negative effect on udder health, when compared with BCLT (Kabera et al., 2020).

Currently, selective cow level programs in the United Kingdom are mainly performed in herds engaged in DHI programs with varying SCC thresholds and strategies used for identifying cows with an IMI at DO. However, SQLT requires a diagnosis at quarter level which is not routinely available. The California Mastitis Test (**CMT**), first described and used in 1957 (Schalm and Noorlander, 1957), has been accepted as a practical, quick, simple, and easy-to-do cow-side test to predict SCC at DO from individual quarters (Sanford et al., 2006). Sanford et al. (2006) reported the negative predictive value of CMT was >95% in herds with low major pathogen IMI prevalence at DO, typically associated with a low BMSCC, so that SQLT might be reasonable for such herds if quarters were screened with CMT.

The objective of this study was to compare antibiotic use and dry period outcomes of SQLT and SCLT, in dairy herds in the United Kingdom, using CMT to determine infection status at the quarter level at DO. Our hypothesis was that selecting antibiotic dry cow therapy at the quarter rather than cow level could further refine antibiotic use without detriment to udder health.

MATERIALS AND METHODS

This study was conducted under Animal Test Certificate No: ATC-S-084 under The Veterinary Medicines Regulations 2013 SI 2013/2033 issues by the Veterinary Medicines Directorate, Surrey, United Kingdom.

Herd Selection

Six commercial farms with conventional milking systems in the southwest of England were selected to participate based on likely compliance with the study protocol, a low prevalence of contagious pathogens based on historical clinical knowledge of these herds, showing classic contagious pathogens such as *S. aureus* representing less than 5% of all major pathogen infections, and with no infections with *Streptococcus agalactiae* for at least 10 yr, a history of BMSCC less than 250,000 cells/mL (milk sold off farm) in the past 12 mo, monthly individual cow SCC testing, and retrospective records of clinical mastitis (**CM**) for at least 12 mo. Cows were managed according to normal husbandry practices on the farm. On each farm, farm-specific data such as BMSCC, herd size, management, and housing data were collated.

Cow Selection

Cows were enrolled before their final milking in lactation and assessed for suitability for enrollment, over a 12-mo period, from July 2017 to July 2018, to allow seasonal effects to be investigated. Animals were eligible for enrollment if, according to study personnel, based on an assessment of farm records and a clinical inspection they were in good general health, had 4 functional quarters, and had been enrolled on a monthly SCC scheme for at least the 3 preceding months. Animals were not eligible for enrolling if they had intercurrent disease based on physical inspection, were expected to calve within the minimum dry period of 32-d withdrawal time as labeled for CEFA-SAFE Dry Cow (MSD Animal Health), or had received parenteral or intramammary treatment with an antibacterial or antiinflammatory medication during a 30-d period immediately before recruitment to the study. Animals were withdrawn from the study and censored in any analysis based on welfare grounds (i.e., disease, injury, or disability), or in case of any abnormality (other than mastitis) requiring AB or antiinflammatory treatment during the dry period and the first 100 d of the subsequent lactation.

Study Protocol

Enrollment. Farms were visited weekly by a member of the research team. At enrollment, key cow parameters were collated from farm records, including, but not limited to, breed, parity, milk yield, SCC and CM history, treatment history, and estimated calving date. Before the final milking and before treatment allocation and administration, each animal was assessed for suitability for inclusion in the study based on inclusion and exclusion criteria. Cows were then randomly selected for inclusion in the study based on the need to recruit cows in equal numbers, on each farm, on the basis of their SCC category (see below). On each day of recruitment, all cows eligible to be dried off were presented by the farmer. The farmer was blinded to the methods of cow recruitment. These cows were then sorted, by study personnel, by ascending line number and recruited in blocks of 6 animals, 3 to each SCC category. Significant numbers of low SCC cows were not recruited as they tended to outnumber cows in the high SCC category.

Teat end callosity (**TEC**) scores (Neijenhuis et al., 2000) and a BCS was performed according to the DairyCo Guide, available at https://ahdb.org.uk/knowledge-library/body-condition-scoring-flow-chart.

Duplicate milk samples were collected aseptically for bacteriology and a single sample for SCC determination was collected from each quarter of each recruited cow using a method described previously (Bradley and Green, 2000). A CMT test was also performed, cow side, on each quarter following a method and scoring previously described (Leach et al., 2008); any reaction was scored on a range from 0 to 3, where 0 represented no evidence of thickening or gel formation, 1 a trace reaction (slight thickening of the liquid forms but no gel formation), 2 a weak positive (thickens immediately and gel formation is suggested), and 3 a distinct or strong positive (a clear gel is formed).

Treatment Allocation and Administration. The overall allocation of cows to treatment groups is summarized in Figure 1. At DO, cows were categorized as high or low SCC based on CM and SCC history. Cows with any of the last 3 monthly individual SCC $\geq$200,000 cells/mL or an occurrence of CM within that period were categorized to the high SCC group; all other cows (i.e., with low SCC and no CM) were categorized to the low SCC group.

Within each of the 2 categories cows were randomly allocated, by study personnel, based on a randomized, pre-allocated order of treatment group within recruitment blocks. Farm personnel were blinded to product administration. These 3 treatment groups comprised either SCLT where all quarters received the same treatment or quarter level treatment allocation where AB treatment was applied at the quarter level according to a CMT score. In the SQLT groups, treatments were allocated using a CMT score threshold of 1 (**SQLT1**) or 2 (**SQLT2**). Because both the high SCC (**H**) and low SCC (**L**) category cows contained these 2 quarter level groups, we abbreviated them as **H-SQLT1**, **H-SQLT2** and **L-SQLT1**, **L-SQLT2**.

All treatments were administered following strict asepsis, according to datasheet recommendations by a member of the study team. When cows or quarters were eligible to receive AB treatment, an intramammary AB (cephapirin benzathine, 300 mg, CEFA-SAFE, MSD Animal Health) was administered before applying the teat sealant in the same quarter. All quarters of all cows in the study received an internal teat sealant (Bismuth subnitrate, 2.6 g, and povidone, CEPRALOCK, MSD Animal Health).

When treatments were allocated at the cow level (SCLT), cows in the high SCC category received AB in all 4 quarters before an internal teat sealant, whereas all 4 quarters in cows in the low SCC category received an internal teat sealant alone. When treatments were allocated at the quarter level (SQLT), all quarters still received an internal teat sealant, but AB treatment was indicated by the CMT score, with the threshold differing for the SQLT1 and SQLT2 groups, regardless of SCC category.

Two different quarter level CMT score thresholds were used to facilitate investigation of the most appropriate threshold for optimizing dry period outcomes and AB use. Irrespective of SCC category, quarters in cows allocated to the SQLT1 group received AB treatment if a quarter CMT showed at least a trace reaction (score ≥1). Quarters of cows assigned to the SQLT2 group received AB treatment when a quarter CMT showed at least a weak positive reaction (score ≥2).

Dry Period Management. Following DO, cows were managed according to the normal husbandry practices for each of the study farms. Any concurrent treatments were recorded, and CM cases sampled for bacteriology by farm personnel trained in aseptic sample collection.

Postcalving. Experienced, trained study personnel took duplicate aseptic milk samples for bacteriology and a single sample for SCC from each quarter at the first weekly visit after calving. Samples collected more than 10 d after calving were excluded from the analysis of efficacy as measured by the cure and acquisition of IMI during the dry period. In addition, cows were scored for BCS and quarters for TEC. At the second weekly visit postcalving, quarters were again sampled for SCC determination.

Calving to 100 DIM. All CM cases were sampled and recorded by trained farm personnel; samples were then frozen on farm until collection at the weekly visit. Details of any other disease or concurrent treatments were collated as were DHI data relating to monthly milk production and individual cow SCC.

Laboratory Methods. All milk samples collected were maintained at or below 8°C during transport to the laboratory for analysis. Microbiological investigation and SCC were carried out in accordance with the methods recommended by the International Dairy Federation (IDF, 1981; Bulletin No. 132), and International standard 13366-1: 1997 (E) and 13366-2: 1997 (G). In summary, samples were inoculated onto blood, MacConkey, and Edwards agar and incubated for 72 h at 37°C. Both the blood and Edwards agar were inoculated with 10 μL of milk. The MacConkey agar was inoculated with 100 μL of milk to enhance the chances of isolation of *Enterobacteriaceae*. All organisms were identified and enumerated. Organisms were identified primarily by using MALDI-TOF MS, but also, where

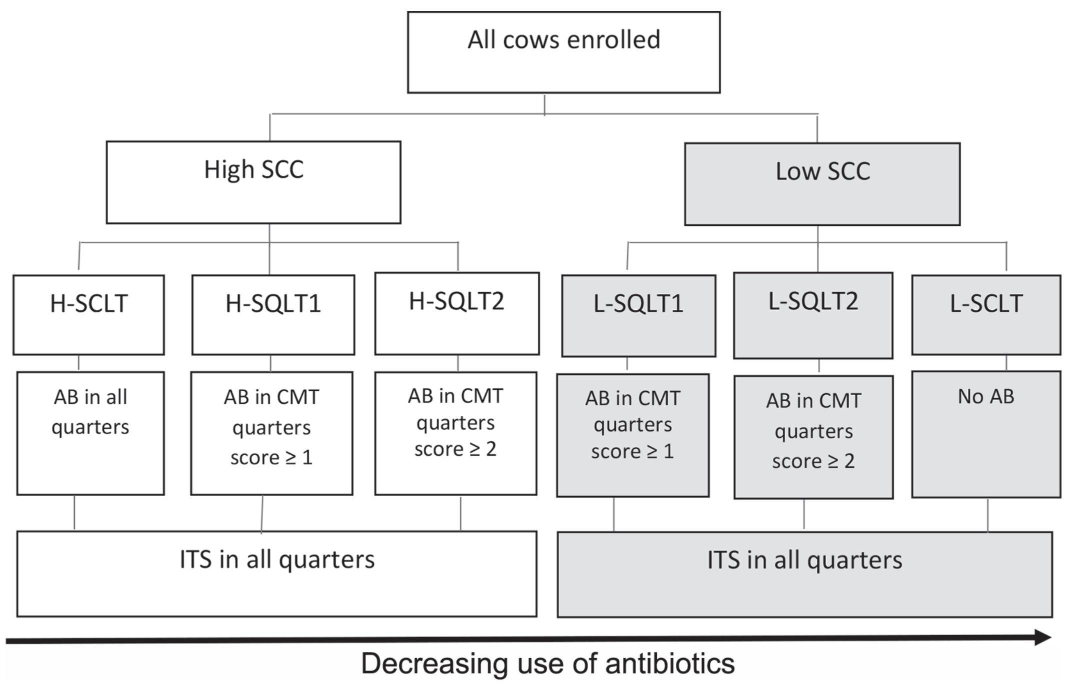

Figure 1. Overview of the study design and overall allocation of cows to treatment groups, from a study in the United Kingdom comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows. Eight hundred seven cows were recruited to the study at drying off (DO), of which 766 calved, and 764 were available for analysis. High SCC cows: any of the last 3 monthly individual cow SCC ≥200,000 cells/mL, before DO, or any clinical mastitis case occurring in the time period from the day of the third monthly individual cow SCC test before DO, to the day of DO. Low SCC cows: all of the last 3 monthly individual cow SCC <200,000 cells/mL, before DO, and no clinical mastitis occurred from the day of the third monthly individual cow SCC test before DO to the day of DO. L- = low SCC category at DO; H- = high SCC category at DO. SCLT = selective cow level treatment; SQLT1 = selective quarter level treatment CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1); SQLT2 = selective quarter level treatment CMT positive, at least a weak positive (CMT score ≥2); AB = antibiotic; ITS = internal teat sealant.

necessary, based on typical colony morphology, Gram staining, and further biochemical tests. Isolation of an organism in pure or mixed growth was considered indicative of an IMI. A sample was considered contaminated if >3 pathogens were cultured from a sample. If this occurred, the duplicate sample was submitted for bacteriological analysis (Bradley and Green, 2000).

For the purposes of analysis, *Corynebacterium* spp., CNS (excluding coagulase-negative *S. aureus*), and other closely related species were considered minor mastitis pathogens. For a full breakdown of bacterial classifications, see Supplemental Table S1 (http://dx.doi.org/10.17632/4hsr7gykzd.1).

Somatic cell count was determined using the Fossomatic method (Delta CombiScope–Model FTIR 400, Delta Instruments) according to the FIL IDF 148 A: 95 norm (IDF, 1995).

Assessment of Efficacy. The primary outcomes considered were related to bacteriological status at calving and the rate of CM mastitis in the first 100 DIM in the subsequent lactation, when compared between treatment groups within infection categories.

The overall and species-specific cure rates were estimated and compared between groups. A cure was defined as the absence of a pathogen at calving that had been present at DO. The overall and species-specific new infection rates were estimated and compared between groups. A new infection was defined as the presence of a pathogen at calving that had not been present at DO. Therefore, a quarter infected with a pathogen at DO was eligible to acquire a new infection with a different pathogen.

Successful dry period outcomes were estimated and compared between groups. A successful outcome was explored in 2 ways: (1) the absence of a major pathogen from the postcalving sample, and (2) the absence of minor mastitis pathogen from the postcalving sample.

The overall and species-specific incidence rate of CM was assessed in the first 100 DIM lactation and compared between products.

In addition, the effect of the different strategies on SCC and milk yield in early lactation and on AB use was considered.

Data Collation and Statistical Analysis

Power and sample size calculations based on UK data suggested that assuming 80% power and 95% confidence in a 2-sided test the proposed sample sizes would allow detection of a ≥6% (absolute) difference in a successful dry period outcome, given a baseline level of 70% of quarters being pathogen free postcalving in the SCLT group. Both univariable and multivariable analysis were conducted.

Data were collated and initially analyzed using Excel and Access (Microsoft Corp.) and Minitab (Minitab Inc.). Descriptive and graphical analyses were carried out to explore the data. Univariable analysis of treatment efficacy was performed using the chi-square test to investigate differences in proportions between groups. A layered Bonferroni correction was used to allow for multiple comparisons where appropriate (Darlington, 1990). Analysis was undertaken assessing high SCC and low SCC cows both separately and together.

Multilevel logistic regression models were specified with the response variables: (1) absence of a major pathogen postcalving, (2) absence of a minor pathogen postcalving, (3) cow level SCC at the first DHI test in lactation, or (4) CM on one or more occasions, within the first 100 DIM. Random effects were included for cow (level 2) and farm (level 3) to account for correlations within the data (i.e., quarters within cows and cows within farms). Potential confounding factors such as milk yield and infection status at DO, quarter location, TEC score, BCS, dry period length, season of calving, and parity were tested and included in final models if they influenced the treatment effect (>5% change in coefficient). The models took the following general form:

$$\mathrm{Response}_{ijk} \sim \mathrm{Bernoulli}(\mathrm{probability} = \mu_{ijk})$$

$$\mathrm{logit}(\mu_{ijk}) = \alpha + \beta_1 \mathrm{TX}_{ijk} + \beta_2 \mathrm{X}_{ijk} + \beta_3 \mathrm{X}_{jk} + \beta_4 \mathrm{X}_k \mathrm{v}_k + \mathrm{u}_{jk},$$

where v_k ~normal distribution (mean = 0, σ_v^2), u_{jk} ~normal distribution (mean = 0, σ_u^2), the subscripts i, j, and k denote the ith quarter, the jth cow, and the kth farm, respectively; μ_{ijk} = the fitted probability of the response in quarter i of cow j in farm k; α = the regression intercept; TX_{ijk} = covariate treatment; β_1 = coefficients for TX_{ijk}; X_{ijk} = matrix of quarter level covariates; β_2 = coefficients for X_{ijk}; X_{jk} = matrix of cow level covariates; β_3 = coefficients for X_{jk}; X_k = matrix of farm level covariates; β_4 = coefficients for X_k; v_k = random effect reflecting residual variation between farms; u_{jk} = random effect reflecting residual variation between quarters of cows; σ_v^2 = between farm variance; and σ_u^2 = between cow variance. Model building, parameter estimation, and assessment of model fit were performed in MLwiN version 2.10 (Rasbash et al., 2009).

Table 1. Key characteristics of the 6 study farms in the United Kingdom, where selective dry cow treatment at cow level was compared with quarter level

Variable	Farm					
	C	F	H	M	R	T
Herd size (number of cows in milk)	730	225	249	150	223	580
Number of cows enrolled	250	93	113	46	100	205
12-mo geometric mean BMSCC[1]	122	171	146	155	237	313
Clinical mastitis incidence in 12 mo before study start[2]	20	34	74	42	77	23
305-d milk yield (L) at study start[3]	10,115	9,975	8,790	7,633	7,716	10,878
Predominant breed[4]	HF	HF	HF	HFX	HF	HF
Dry cow winter housing[5]	C, Y	C, Y	Y	C, Y	C, Y	C, Y
Dry cow summer housing[5]	P	C, Y	P	P	P	Y
Dry cow bedding	Sand	Sand	Straw	Straw	Straw	Straw
Milking frequency/d	3×	2×	2×	2×	2×	3×

[1]Calculated bulk milk SCC (× 1,000/mL) based on individual cow recording.

[2]Cases/100 cows per year.

[3]Cows and heifers.

[4]HF = Holstein Friesian; HFX = Holstein Friesian Cross.

[5]C = cubicles; Y = yards; P = pasture.

RESULTS

Key characteristics of the 6 study herds are shown in Table 1. From these herds, 807 cows were recruited to the study at DO of which 766 cows calved and data of 764 cows were available for analysis, of which 381 cows were categorized as high SCC, and 383 categorized as low SCC. In the high SCC category, the number of cows for each of the 3 treatment groups was H-SCLT (n = 126), H-SQLT1 (n = 122), and H-SQLT2 (n = 133) and in the low SCC category; L-SCLT (n = 125), L-SQLT1 (n = 128), and L-SQLT2 (n = 130) (Figure 1). A summary of cow and quarter level data is shown in Table 2. No significant differences were identified between the 3 groups within the high SCC and low SCC categories ($P > 0.05$).

Univariable Analysis

Prevalence of Infection at DO. The prevalence of key mastitis pathogens and pathogen groups at DO and calving by treatment group in cows categorized as high and low SCC at DO are summarized in Tables 3 and 4, respectively. When comparing within SCC category

Table 2. Summary of mean (and SD) cow and quarter level data of the 3 treatment groups within each SCC category at drying off (DO; high and low SCC), in descending use of antibiotics from left to right, from a study in the United Kingdom comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level[1,2]

Item	High SCC			Low SCC		
	H-SCLT	H-SQLT1	H-SQLT2	L-SQLT1	L-SQLT2	L-SCLT
Cow level DO						
n (cows)	126	122	133	128	130	125
Parity	2.55 (1.37)	2.60 (1.48)	2.48 (1.39)	2.11 (1.34)	2.18 (1.17)	2.00 (1.23)
Milk yield (L)	16.4 (8.58)	16.8 (9.32)	17.0 (9.67)	17.7 (7.98)	18.3 (8.18)	18.7 (8.23)
BCS	2.98 (0.58)	3.00 (0.62)	2.99 (0.57)	2.83 (0.55)	2.87 (0.52)	2.96 (0.60)
Cow lnSCC 1 mo before DO	5.51 (0.93)	5.57 (1.01)	5.63 (0.80)	4.19 (0.79)	4.12 (0.72)	4.08 (0.69)
Cow lnSCC 2 mo before DO	5.32 (0.93)	5.28 (1.06)	5.32 (0.80)	3.99 (0.66)	3.94 (0.69)	3.87 (0.65)
Cow lnSCC 3 mo before DO	5.21 (1.21)	5.13 (1.10)	5.17 (1.14)	3.88 (0.78)	3.66 (0.68)	3.78 (0.71)
Dry period length (d)	57.8 (24.5)	54.0 (16.6)	57.2 (26.7)	53.5 (15.2)	53.4 (18.3)	54.5 (18.6)
Quarter level DO						
n (quarters)	504	488	532	512	520	500
CMT score	1.23 (1.02)	1.30 (1.07)	1.23 (1.08)	0.43 (0.73)	0.45 (0.74)	0.39 (0.69)
TEC score	1.85 (0.69)	1.85 (0.72)	1.95 (0.76)	1.74 (0.65)	1.76 (0.64)	1.73 (0.66)
lnSCC	5.65 (1.39)	5.55 (1.45)	5.65 (1.42)	4.41 (1.24)	4.39 (1.25)	4.30 (1.20)

[1]Differences between treatment groups within SCC category were not significant ($P > 0.05$).

[2]L- = low SCC category at DO; H- = high SCC category at DO. SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant when high SCC at DO, and a teat sealant only when low SCC at DO. SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2). TEC = teat end callosity.

(i.e., high or low SCC), no significant differences ($P > 0.05$) were observed between treatment groups in the high SCC category at DO. However, in the low SCC category, when allowances had been made for multiple comparisons, quarters in the L-SQLT1 treatment group were significantly less likely to yield no growth on culture than quarters in the L-SCLT (223/512 vs. 258/500; $P = 0.03$) and L-SQLT2 (223/512 vs. 265/520; $P = 0.03$) groups.

Apparent Dry Period Cure Rate. The apparent dry period cure rates for key mastitis pathogens and pathogen groups are summarized in Table 5. In the high SCC cow category, no significant differences in apparent cure rates for major pathogens were identified, though the apparent cure rate for minor mastitis pathogens was significantly lower in the H-SQLT2 treatment group than in the H-SCLT (268/305 vs. 283/290; $P < 0.001$) or H-SQLT1 (268/305 vs. 272/284; $P = 0.002$) treatment groups. This was primarily as a result of the difference in the apparent cure rate for minor coryneform mastitis pathogens, which was significantly lower in the H-SQLT2 treatment group than in H-SCLT (184/218 vs. 199/205; $P < 0.001$) or H-SQLT1 (184/205 vs. 195/205; $P < 0.001$), as the apparent cure rates for minor coccal mastitis pathogens did not differ.

Similarly, in the low SCC cow category, no significant differences in apparent cure rates for major pathogens were identified, though the apparent cure rate for minor coryneform mastitis pathogens was significantly lower in the L-SCLT treatment group than in the L-SQLT1 (74/135 vs. 124/169; $P = 0.003$) or L-SQLT2 (74/135 vs. 97/141; $P = 0.034$) treatment groups.

Apparent Dry Period New Infection Rate. The apparent dry period new infection rates for key mastitis pathogens and pathogen groups are summarized in Table 6. Whereas trends were evident between treatment groups in the apparent new infection rate for major mastitis pathogens in the low SCC category, no significant differences were identified for any of the pathogen or pathogen groups tested in either SCC category.

Dry Period Outcomes. When comparing treatment groups at calving, within the high SCC category (Table 3) no significant differences were identified, with the exception that quarters in cows in the H-SCLT group were significantly less likely to be infected with a minor coryneform organism than quarters in the H-SQLT2 group (34/504 vs. 75/532, $P < 0.001$). In the low SCC category (Table 4), quarters in cows in the L-SCLT group were significantly less likely to be free of any pathogen (228/500 vs. 279/512; $P = 0.015$) and significantly more likely to be infected with a minor mastitis pathogen (208/500 vs. 175/520; $P = 0.045$) than quarters in cows in the L-SQLT1 group. Quarters in cows in the L-SQLT2 group were also significantly more likely to be infected with a major mastitis pathogen than quarters in cows in the L-SQLT1 group (70/520 vs. 43/512; $P = 0.027$).

Clinical Mastitis. The rates of CM in all groups were low with between 4.65% (low SCC category L-SQLT1) and 5.75% (low SCC category L-SCLT) of quarters affected in the first 100 DIM. Environmental pathogens predominated and only 3 cases of *S. aureus* mastitis occurred in study cows. No significant differences were detected between treatment groups ($P > 0.5$).

Postcalving SCC and Milk Yield. The effect of treatment group on quarter SCC was similar in both the first and second week after calving, with increasingly liberal use of intramammary AB associated with lower quarter SCC after calving. In the high SCC cow category quarters in cows in the H-SQLT2 group had significantly higher lnSCC than quarters in cows in the H-SQLT1 (4.08 vs. 3.80; $P = 0.006$) and H-SCLT (4.08 vs. 3.74; $P < 0.001$) groups in the second week after calving. In the low SCC cow category quarters in cows in the L-SCLT group had significantly higher lnSCC than quarters in cows in the L-SQLT2 (4.14 vs. 3.82; $P = 0.006$) and L-SQLT1 (4.14 vs. 3.76; $P < 0.001$) groups in the second week after calving. The effect of treatment on cow level SCC at the first DHI test after calving is summarized in Table 7. No significant differences were identified between treatment groups in the cows defined as high SCC at DO; however, in the low SCC category, cows in the L-SCLT group had significantly higher lnSCC than cows in the L-SQLT1 group (4.23 vs. 3.75; $P = 0.03$). Cumulative milk yields of the first 100 DIM were compared between treatment strategies within SCC category. Mean milk yields were 3,968 L (H-SCLT), 3,976 L (H-SQLT1), and 3,779 L (H-SQLT2) when high SCC at DO, and 3,896 L (L-SCLT), 4,015 L (L-SQLT1), and 4,005 L (L-SQLT2) when low SCC at DO. No significant differences were identified between treatment groups with infection categories.

Effect on Use of Antibiotic Dry Cow Treatment. The number of AB tubes used in each treatment group within each category was calculated and compared with the number of quarters cured of bacterial IMI. The findings of this analyses are summarized in Table 8. In the high SCC category, significantly fewer AB intramammary tubes were used per cure in the H-SQLT2 and H-SQLT1 treatment groups than in the H-SCLT group (3.87 vs. 10.12; $P < 0.001$ and 5.06 vs. 10.12; $P < 0.001$, respectively), but the number of tubes used per cure did not differ between the quarter level treatment groups. Similarly, in the low SCC category, significantly more AB intramammary tubes were used per cure in the L-SQLT1 and L-SQLT2 treatment groups than in the L-SCLT group (3.24 vs. 0.00; P

Table 3. Summary of the prevalence of infection at drying off and postcalving of the 3 different treatment groups, in cows in the high SCC cow category at drying off from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows[1]

	At drying off								Postcalving							
	H-SCLT		H-SQLT1		H-SQLT2		Overall		H-SCLT		H-SQLT1		H-SQLT2		Overall	
Item	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
n	504		488		532		1,524		504		488		532		1,524	
Staphylococcus aureus	4	0.79	9	1.84	4	0.75	17	1.12	2	0.40	4	0.82	0	0.00	6	0.39
Streptococcus uberis	4	0.79	9	1.84	6	1.13	19	1.25	5	0.99	12	2.46	7	1.32	24	1.57
Streptococcus dysgalactiae	3	0.60	2	0.41	1	0.19	6	0.39	0	0.00	2	0.41	3	0.56	5	0.33
Lactococcus spp.	8	1.59	13	2.66	21	3.95	42	2.76	2	0.40	8	1.64	10	1.88	20	1.31
Enterococcus spp.	4	0.79	3	0.61	5	0.94	12	0.79	4	0.79	1	0.20	4	0.75	9	0.59
Escherichia coli	2	0.40	2	0.41	3	0.56	7	0.46	3	0.60	3	0.61	0	0.00	6	0.39
Fungal spp.	0	0.00	0	0.00	1	0.19	1	0.07	0	0.00	2	0.41	0	0.00	2	0.13
Yeast spp.	2	0.40	5	1.02	5	0.94	12	0.79	7	1.39	8	1.64	8	1.50	23	1.51
All *Enterobacteriaceae*	4	0.79	3	0.61	3	0.56	10	0.66	4	0.79	5	1.02	10	1.88	19	1.25
Gram-positive major pathogens	43	8.53	61	12.50	54	10.15	158	10.37	36	7.14	48	9.84	46	8.65	130	8.53
Gram-negative major pathogens	12	2.38	13	2.66	13	2.44	38	2.49	20	3.97	22	4.51	21	3.95	63	4.13
Minor coryneform spp.	208	41.27	205	42.01	218	40.98	631	41.40	34	6.75[a]	47	9.63[ab]	75	14.10[b]	156	10.24
Minor coccal spp.	134	26.59	119	24.39	123	23.12	376	24.67	110	21.83	100	20.49	124	23.31	334	21.92
All major pathogens	56	11.11	73	14.96	71	13.35	200	13.12	59	11.71	75	15.37	72	13.53	206	13.52
All minor pathogens	293	58.13	284	58.20	306	57.52	883	57.94	135	26.79	136	27.87	178	33.46	449	29.46
Contaminated	2	0.40	3	0.61	2	0.38	7	0.46	6	1.19	1	0.20	2	0.38	9	0.59
No growth	187	37.10	165	33.81	191	35.90	543	35.63	296	58.73	277	56.76	275	51.69	848	55.64

[a,b]Different superscripts within a row and within SCC category differ ($P \leq 0.05$).

[1]H- = high SCC category at drying off. H-SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant. H-SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). H-SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

Table 4. Summary of the prevalence of infection at drying off and postcalving of the 3 different treatment groups, in cows in the low SCC cow category at drying off, from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows[1]

	At drying off								Postcalving							
	L-SCLT		L-SQLT2		L-SQLT1		Overall		L-SCLT		L-SQLT2		L-SQLT1		Overall	
Item	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
n	500		512		520		1,532		500		512		520		1,532	
Staphylococcus aureus	0	0.00	5	0.96	4	0.78	9	0.59	1	0.20	2	0.38	1	0.20	4	0.26
Streptococcus uberis	1	0.20	1	0.19	0	0.00	2	0.13	8	1.60	12	2.31	6	1.17	26	1.70
Streptococcus dysgalactiae	0	0.00	0	0.00	0	0.00	0	0.00	2	0.40	0	0.00	2	0.39	4	0.26
Lactococcus spp.	2	0.40	5	0.96	4	0.78	11	0.72	1	0.20	2	0.38	2	0.39	5	0.33
Enterococcus spp.	1	0.20	0	0.00	0	0.00	1	0.07	5	1.00	2	0.38	3	0.59	10	0.65
Escherichia coli	0	0.00	3	0.58	2	0.39	5	0.33	6	1.20	5	0.96	3	0.59	14	0.91
Fungal spp.	0	0.00	0	0.00	1	0.20	1	0.07	1	0.20	0	0.00	0	0.00	1	0.07
Yeast spp.	4	0.80	4	0.77	1	0.20	9	0.59	3	0.60	8	1.54	1	0.20	12	0.78
All *Enterobacteriaceae*	2	0.40	3	0.58	2	0.39	7	0.46	10	2.00	8	1.54	6	1.17	24	1.57
Gram-positive major pathogens	24	4.80	25	4.81	34	6.64	83	5.42	31	6.20	40	7.69	29	5.66	100	6.53
Gram-negative major pathogens	8	1.60	10	1.92	20	3.91	38	2.48	16	3.20	26	5.00	16	3.13	58	3.79
Minor coryneform spp.	135	27.00	142	27.31	170	33.20	447	29.18	101	20.20	95	18.27	83	16.21	279	18.21
Minor coccal spp.	124	24.80	115	22.12	120	23.44	359	23.43	121	24.20	103	19.81	106	20.70	330	21.54
All major pathogens	34	6.80	37	7.12	51	9.96	122	7.96	48	9.60^{ac}	70	13.46^{a}	43	8.40^{bc}	161	10.51
All minor pathogens	228	45.60	236	45.38	265	51.76	729	47.58	208	41.60^{ac}	184	35.38^{bc}	175	34.18^{b}	567	37.01
Contaminated	4	0.80	1	0.19	0	0.00	5	0.33	0	0.00	1	0.19	1	0.20	2	0.13
No growth	258	51.60^{a}	265	50.96^{a}	223	43.55^{b}	746	48.69	228	45.60^{a}	253	48.65^{ab}	279	54.49^{b}	760	49.61

[a–c]Different superscripts within a row and within SCC category differ ($P \leq 0.05$).

[1]L- = low SCC category at drying off. L-SCLT = selective cow level treatment, all quarters of cows receiving a teat sealant. L-SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). L-SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

< 0.001 and 2.03 vs. 0.00; $P < 0.001$, respectively), although the number of tubes used per cure also differed between the L-SQLT1 and L-SQLT2 quarter level treatment groups (3.24 vs. 2.03; $P = 0.009$). The relationship between AB tube usage, major pathogen apparent cure rate, and major and minor pathogen new IMI rates is illustrated in Figure 2. In the high SCC cow category, the proportion of quarters treated with AB reduces from 100% at cow level (H-SCLT) to 69% (H-SQLT1) and 45% (H-SQLT2) at quarter level. In the low SCC cow category, the proportion of quarters treated with AB increases from 0% at cow level (L-SCLT) to 12% (L-SQLT2) and 31% (L-SQLT1) at quarter level.

Multivariable Analysis

Dry Period Outcomes. Two dry period outcomes were modeled: the likelihood of a quarter being free of a major mastitis pathogen and free of a minor mastitis pathogen in the high and low SCC categories. In the high SCC category, compared with the H-SCLT group, the quarter level odds of being infected with a major or minor mastitis pathogen was not affected by selection of AB. Similarly, in the low SCC category, the odds of being infected by a major pathogen did not differ between treatment groups. However, differences were identified in the likelihood of infection with a minor pathogen and are summarized in Table 9; compared with the L-SCLT group, quarters in the L-SQLT1 group were at significantly decreased odds of being infected with a minor pathogen (OR 0.66; 95% CI 0.49 to 0.89), whereas the L-SQLT2 group did not differ (OR 0.76; 95% CI 0.57 to 1.02). Compared with quarters in cows on the farm with the lowest BMSCC, farm C, quarters in cows on 3 farms (F, H, and M) were at significantly increased odds of being infected with a minor pathogen at calving; last 24 h milk yield and the presence of a coryneform at DO were also found to be influential.

Clinical Mastitis. The likelihood of CM in the first 100 DIM was modeled to take into account the potential effect of confounding factors. No significant

Table 5. Summary of the apparent dry period cure rates for key mastitis pathogens and groups in the different treatment groups within the infection categories defined at drying off, in descending use of antibiotics from left to right, from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows[1]

	High SCC at drying off								Low SCC at drying off							
	H-SCLT		H-SQLT1		H-SQLT2		Overall		L-SQLT1		L-SQLT2		L-SCLT		Overall	
Item	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Staphylococcus aureus	4	75.00	9	77.78	4	100.00	17	82.35	4	100.00	5	100.00	0	—	9	100.00
Streptococcus uberis	4	100.00	9	88.89	6	100.00	19	94.74	1	100.00	2	100.00	1	100.00	4	100.00
Streptococcus dysgalactiae	3	100.00	2	100.00	1	100.00	6	100.00	0	—	0	—	0	—	0	—
Lactococcus spp.	8	100.00	13	100.00	21	85.71	42	92.86	4	100.00	5	100.00	2	100.00	11	100.00
Enterococcus spp.	4	100.00	3	100.00	5	100.00	12	100.00	0	—	0	—	1	0.00	1	0.00
Escherichia coli	2	100.00	2	100.00	3	100.00	7	100.00	3	100.00	5	80.00	2	100.00	10	90.00
Fungal spp.	0	—	0	—	1	100.00	1	100.00	1	100.00	0	—	0	—	1	100.00
Yeast spp.	2	100.00	5	80.00	5	20.00	12	58.33	1	100.00	4	75.00	4	100.00	9	88.89
All *Enterobacteriaceae*	4	100.00	3	100.00	3	100.00	10	100.00	2	100.00	3	66.67	2	100.00	7	85.71
Gram-positive major pathogens	42	95.24	61	96.72	53	96.23	156	96.15	34	100.00	25	100.00	24	95.83	83	98.80
Gram-negative major pathogens	12	91.67	13	100.00	13	100.00	38	97.37	20	100.00	10	90.00	8	100.00	38	97.37
Minor coryneform spp.	205	97.07[a]	205	95.12[ac]	218	84.40[bc]	628	92.04	169	73.37[a]	141	68.79[a]	135	54.81[b]	445	66.29
Minor coccal spp.	134	97.01	119	98.32	122	95.08	375	96.80	120	95.83	114	96.49	124	94.35	358	95.53
All major pathogens	55	94.55	73	95.89	70	91.43	198	93.94	51	100.00	37	94.59	34	97.06	122	97.54
All minor pathogens	290	97.59[a]	284	95.77[ac]	305	87.87[bc]	879	93.63	264	81.82	235	80.85	228	75.88	727	79.64

[a–c]Different superscripts within row and within SCC category differ ($P \leq 0.05$).

[1]n = number of quarters cured. L- = low SCC category at drying off, H- = high SCC category at drying off. SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant when high SCC at drying off, and a teat sealant only when low SCC at drying off. SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

Table 6. Summary of the apparent dry period new infection rates for key mastitis pathogens and groups in the different treatment groups within the infection categories defined at drying off, in descending use of antibiotics from left to right, from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows[1]

	High SCC at drying off								Low SCC at drying off							
	H-SCLT		H-SQLT1		H-SQLT2		Overall		L-SQLT1		L-SQLT2		L-SCLT		Overall	
Item	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Staphylococcus aureus	1	0.20	2	0.42	0	0.00	3	0.20	1	0.20	2	0.39	1	0.20	4	0.26
Streptococcus uberis	5	1.02	11	2.32	7	1.34	23	1.54	6	1.18	12	2.33	8	1.62	26	1.71
Streptococcus dysgalactiae	0	0.00	2	0.41	3	0.57	5	0.33	2	0.39	0	0.00	2	0.40	4	0.26
Lactococcus spp.	2	0.41	8	1.70	7	1.38	17	1.16	2	0.39	2	0.39	1	0.20	5	0.33
Enterococcus spp.	4	0.81	1	0.21	4	0.76	9	0.60	3	0.59	2	0.39	4	0.81	9	0.59
Escherichia coli	3	0.61	3	0.62	0	0.00	6	0.40	3	0.59	5	0.97	6	1.21	13	0.86
Fungal spp.	0	0.00	2	0.41	0	0.00	2	0.13	0	0.00	0	0.00	1	0.20	1	0.07
Yeast spp.	7	1.41	6	1.24	4	0.76	17	1.13	1	0.20	7	1.35	3	0.60	11	0.72
All *Enterobacteriaceae*	4	0.81	5	1.03	10	1.89	19	1.26	6	1.17	7	1.35	10	2.02	23	1.51
Gram-positive major pathogens	35	7.06	48	9.92	45	8.52	128	8.49	29	5.68	40	7.72	31	6.25	100	6.56
Gram-negative major pathogens	20	4.03	22	4.55	21	3.98	63	4.18	16	3.13	23	4.44	16	3.23	55	3.61
Minor coryneform spp.	29	5.85	32	6.61	35	6.63	96	6.37	37	7.24	51	9.85	46	9.27	134	8.79
Minor coccal spp.	106	21.37	97	20.04	118	22.35	321	21.29	101	19.77	99	19.11	111	22.38	311	20.39
All major pathogens	58	11.69	72	14.88	69	13.07	199	13.20	43	8.41	66	12.74	48	9.68	157	10.30
All minor pathogens	127	25.60	120	24.79	139	26.33	386	25.60	128	25.05	138	26.64	148	29.84	414	27.15

[1]n = number of quarters acquiring a new IMI. L- = low SCC category at drying off; H- = high SCC category at drying off. SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant when high SCC at drying off, and a teat sealant only when low SCC at drying off. SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2). No significant differences were found between the treatment groups ($P > 0.05$).

Table 7. Summary of individual cow lnSCC at the first DHI test day in lactation in different treatment groups within the different infection categories at drying off (DO), in descending use of antibiotics from top to bottom, from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows

Treatment group[1]	n	Mean	SEM	SD	Minimum	Maximum
High SCC cow category at DO						
H-SCLT	126	3.928	0.129	1.447	1.386	7.902
H-SQLT1	113	3.91	0.137	1.462	1.386	7.757
H-SQLT2	127	4.133	0.139	1.563	1.609	8.793
Low SCC cow category at DO						
L-SQLT1	124	3.751[bc]	0.119	1.33	0.693	8.818
L-SQLT2	127	3.995[ac]	0.133	1.499	1.099	8.46
L-SCLT	122	4.232[a]	0.143	1.581	1.386	8.84

[a–c]Different superscripts within SCC category differ ($P \leq 0.05$).

[1]L- = low SCC category at DO; H- = high SCC category at drying off. SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant when high SCC, and a teat sealant only when low SCC. SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1); SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

differences were identified between treatment groups within either of the infection categories.

Postcalving SCC and Milk Yield. The findings of models investigating the effect of treatment on cow level SCC at the first DHI test for the high and low SCC cow categories are summarized in Tables 10 and 11, respectively. In the high SCC cow category, compared with cows in the H-SCLT group (received AB in all quarters), SCC were significantly higher at the first test day in cows the H-SQLT2 group (only receiving AB in quarters with a CMT ≥ 2). In the low SCC cow category compared with the L-SCLT group (receiving no AB), SCC were significantly lower in the L-SQLT1 group receiving AB in quarters with a CMT ≥ 1).

Models failed to reveal any significant effect of quarter level application of AB dry cow treatment on milk yield in early lactation.

DISCUSSION

This is the first large-scale investigation into the selection of dry cow treatment at quarter level, compared with selection of dry cow treatment at cow level, using CMT to determine infection status at quarter level. Historically, dry cow treatment at quarter level has not been favored due to lack of independence of quarters within cows (Berry et al., 2003). This means the risk of missing a major pathogen infection in another quarter of a high cell count cow is considered too high. For this reason, this study focused on herds with a low prevalence of infection at DO, with classic contagious pathogens such as *S. aureus* representing less than 5% of all major pathogen infections, and with less than 2% of quarters infected with this pathogen at DO, and with no infection of *Streptococcus agalactiae* for the last 10

Table 8. Summary of apparent cure rates and antibiotic tube usage in different treatment groups within infection categories in descending use of antibiotics from top to bottom, from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows

Treatment group[1]	n	Infected at DO	Number cured	Number not cured	Apparent cure rate	Number of antibiotic tubes used	Tubes/cure
High SCC cow category at DO							
H-SCLT	496	53	49	4	92.5	496	10.12[a]
H-SQLT1	484	68	66	2	97.1	334	5.06[b]
H-SQLT2	528	64	62	2	96.9	240	3.87[b]
Low SCC cow category at DO							
L-SQLT1	511	49	49	0	100.0	159	3.24[a]
L-SQLT2	518	33	32	1	97.0	65	2.03[b]
L-SCLT	496	30	29	1	96.7	0	—[c]

[a–c]Different superscripts within a column and within SCC category differ ($P \leq 0.05$).

[1]L- = low SCC category at drying off (DO); H- = high SCC category at DO; SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant when high SCC at DO, and a teat sealant only when low SCC at DO. SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

yr. The etiology in these herds is clearly environmental and minor pathogens were the predominant organisms identified at DO. In such herds, the risk of interdependence of quarters is lower (Barkema et al., 1997) and thus, the probability of missing a major pathogen in another quarter in infected cows is lower too. It was in this environment that efficacy of selective dry cow AB treatment at quarter level, in high and low SCC cows at DO was compared with SCLT.

While not perfect, our categorization of cows as high SCC or low SCC was successful in defining 2 separate groups with significantly different prevalence of infection at DO with significantly more quarters being free of any mastitis pathogen in the low SCC group (48.7%) compared with the high SCC group (35.6%), which was also reflected in the proportion of quarters free of both major and minor mastitis pathogens. This categorization appeared useful as it defined 2 populations within which the use (or not) of AB had different effects. For example, leaving all quarters with a CMT score of <2 in the high SCC group untreated with intramammary antibiotic, resulted in a significant increase in SCC at the first DHI test in the subsequent lactation, whereas intramammary antibiotic treatment in the equivalent quarters in the low SCC group had no significant effect on SCC at the first DHI test in the subsequent lactation.

As with all field studies, there are limitations to this research. One limitation is the fact that it was conducted in a small number of a herds in single geographical location (South West England) with a low prevalence of contagious mastitis pathogens, though we do not see this as limiting how these findings could be generalized to similar herds elsewhere. The study was blinded, and cow randomization was successful, and while farm personnel were blinded to product administration, they could not be fully blinded as product characteristics could have been evident at calving, though it seems unlikely this would have caused any bias. There was no difference in the proportion of cows lost to follow up in any of the treatment groups meaning that bias is unlikely to have been introduced. While this study relied on farmer identification of CM as one of the outcomes, this would not have introduced any bias, as farm personnel were blinded to treatment administration and any shortcomings in their ability would have been reflected across all treatment groups equally.

The data suggest the effect of selecting AB treatment at the quarter level is different in the 2 somatic cell count categories. In the low SCC cows at DO, adding

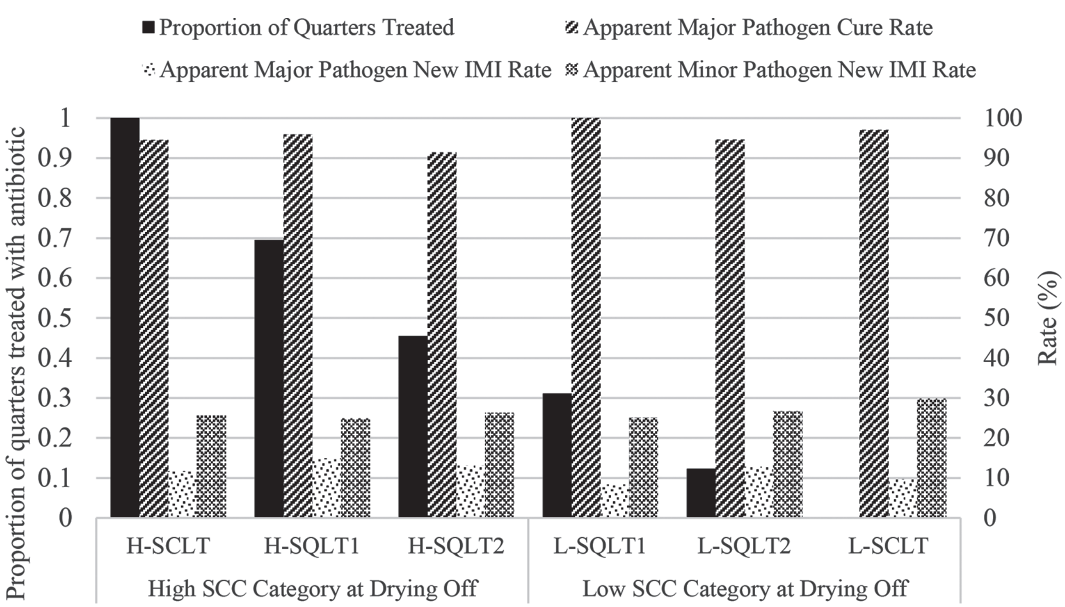

Figure 2. Illustration of the proportion of quarters receiving antibiotic intramammary treatment at drying off and the associated major pathogen cure rate and the major and minor pathogen new infection rate, in each of the treatment groups within SCC category at drying off, in descending use of antibiotic from left to right, from a study in the United Kingdom comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows. L- = low SCC category at drying off; H- = high SCC category at drying off; SCLT = selective cow level treatment, all quarters of cows receiving an antibiotic tube + teat sealant when high SCC at drying off, and a teat sealant only when low SCC at drying off; SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1); SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

Table 9. Summary of the final random effects logistical regression model relating to the likelihood of being infected with a minor mastitis pathogen at calving in cows categorized as low SCC at drying off (DO), from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows

Covariate[1]	Coefficient	SE	Odds ratio	95% CI Lower	95% CI Upper
Intercept	−1.494				
Treatment group					
Antibiotic treatment based on CMT ≥2 (L-SQLT2)	−0.276	0.147	0.76	0.57	1.02
Antibiotic treatment based on CMT ≥1 (L-SQLT1)	−0.418	0.150	0.66	0.49	0.89
Reference: cow level treatment (L-SCLT; sealant only)					
Parity 2	0.109	0.153	1.12	0.82	1.51
Parity 3	−0.025	0.209	0.98	0.64	1.48
Parity ≥4	0.278	0.199	1.32	0.89	1.97
Reference: parity = 1					
Farm F	0.562	0.239	1.75	1.09	2.83
Farm H	0.997	0.283	2.71	1.54	4.77
Farm M	0.899	0.322	2.46	1.29	4.68
Farm R	0.297	0.250	1.35	0.82	2.22
Farm T	−0.014	0.197	0.99	0.66	1.46
Reference: farm C					
Teat score S	0.255	0.146	1.29	0.96	1.73
Teat score R	−0.059	0.211	0.94	0.62	1.44
Teat score VR	−0.619	1.177	0.54	0.05	5.67
Reference: teat score = N					
Left-hind	−0.023	0.159	0.98	0.71	1.34
Right-fore	0.017	0.157	1.02	0.74	1.39
Right-hind	−0.054	0.160	0.95	0.69	1.30
Reference: quarter location left-fore					
Minor coryneform organism present at DO	0.99	0.145	2.69	2.01	3.60
Reference: minor coryneform organism not present at DO					
Minor coccal organism present at DO	0.029	0.137	1.03	0.78	1.35
Reference: minor coccal organism not present at DO					
Summer calving	−0.016	0.175	0.98	0.69	1.40
Autumn calving	−0.270	0.182	0.76	0.53	1.10
Winter calving	−0.292	0.181	0.75	0.52	1.07
Reference: spring calving					
BCS at DO	0.073	0.122	1.08	0.84	1.37
Dry period length	−0.003	0.004	1.00	0.99	1.01
Last milk yield (24 h before DO)	0.024	0.012	1.02	1.00	1.05

[1]L- = low SCC category at DO; L-SQLT1 = selective quarter level antibiotic treatment when CMT (California Mastitis Test) positive, showing at least a trace (CMT score ≥1). L-SQLT2 = selective quarter level antibiotic treatment when CMT positive, showing at least a weak positive (CMT score ≥2).

an AB treatment to a teat sealant in CMT positive quarters, lowered both quarter SCC postcalving and the probability of being infected with a minor pathogen at calving, but had no effect on major pathogen prevalence at calving. Significantly lower SCC and lower prevalence of minor pathogens was the only effect of quarter level treatment compared with cow level in this category. However, in an absolute sense, these improvements in udder health were small; quarter SCC postcalving reduced from 63,000 cells/mL (ln = 4.14) when DO treatment was at cow level (L-SCLT) to 43,000 (ln = 3.76) and 46,000 (ln = 3.82) cells/mL when DO treatment was at quarter level, for the L-SQLT1 and L-SQLT2 group, respectively, while minor pathogen prevalence at calving reduced from 41.60% to 34.18% in the L-SQLT1 group. Also, in this category of low SCC cows at DO, there were no effects on CM incidence nor on cumulative milk yield in the first 100 DIM. These limited improvements in udder health when dried off at quarter level, probably do not justify an increase of AB use from 0% of quarters treated with AB in the L-SCLT group to 12.3% (L-SQLT2) and to 31.1% (L-SQLT1).

In the high SCC cows at DO, leaving CMT negative (score 0) quarters untreated with dry cow antibiotic, was not associated with any significant increase in quarter SCC postcalving. However, leaving quarters untreated with dry cow antibiotic, in which there was no or only a trace reaction (score 0 and 1) to the CMT, was associated with a significant increase in quarter SCC postcalving from 42,000 (ln = 3.74) cells/mL to 60,000 (ln = 4.09) cells/mL. Selective DO off at the quarter level had no effect on minor or major pathogen prevalence at calving in the multivariable model and had no effect on CM incidence and cumulative milk yield in the first 100 DIM. The limited rise in SCC, as a result of withdrawing treatment from CMT-negative quarters compared with cow level treatment, is a relatively small detriment to udder health and when weighed against the substantial reduction in AB use of 31% (H-SQLT1), some degree of quarter level DO seems justifiable compared with cow level in the high SCC cow category (H-SCLT) at DO.

Based on these data we suggest quarter level DO can only be justified for leaving CMT-negative quarters untreated with dry cow antibiotic in high SCC infected cows at DO. This is in line with the findings of others (Patel et al., 2017; Kabera et al., 2020) who found that by DO at quarter level, AB use can be reduced without detriment to udder health. However, these authors compared SQLT with BCLT and used bacteriological culture to determine infection status at DO at the quarter level, whereas in this study SQLT was compared with SDCT, and CMT was used.

Farmers have indicated concern about the extra labor and the financial consequences of switching from blanket to selective dry cow treatment at the cow level (Scherpenzeel et al., 2016). Therefore, both a high convenience and a low price of determining infection status at dry off may remove barriers to adoption of such programs (Friedman et al., 2007). Recently, the use of on-farm culture systems such as 3M Petrifilm (Cameron et al., 2014; Kabera et al., 2020) and the Minnesota Easy 4Cast (Patel et al., 2017; Rowe et al., 2020a,b) were used to determine infection status at dry off, assuming culture would have a higher sensitivity and specificity, compared with indirect tests such as SCC. However, Rowe at al. (2020a,b) showed an algorithm-guided cow-level test method based on SCC and CM history was as good as an on-farm culture system in achieving favorable dry period outcomes and antibiotic use reduction when compared with on-farm culture guided SDCT. If as good as on-farm culture, an algorithm guided diagnosis to detect infection status at DO, based on SCC and CM history, such as in this study, is preferable because of the higher convenience and lower price compared with on-farm culture. Because the algorithms used to determine infection at DO vary widely between studies, some being more (Rowe et al., 2020a,b) or less strict (Scherpenzeel et al., 2014) when compared with this study, more research is needed on this topic to optimize such algorithms.

High convenience and low price of diagnostic tests at DO become even more relevant in selective dry cow

Table 10. Summary of the final random effects logistical regression model relating to the effect of treatment group on the individual cow SCC at the first DHI test in lactation in cows categorized as high SCC at drying off (DO), from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows

			95% CI	
Covariate[1]	Coefficient	SE	Lower	Upper
Intercept	0.057			
Treatment group				
Sealant-only treatment based on CMT <2 (H-SQLT2)	0.307	0.092	0.123	0.491
Sealant-only treatment based on CMT <1 (H-SQLT1)	0.135	0.094	−0.053	0.323
Reference: cow level treatment (H-SCLT; antibiotic + sealant)				
Parity 2	−0.018	0.107	−0.232	0.196
Parity 3	−0.181	0.123	−0.427	0.065
Parity ≥4	0.595	0.119	0.357	0.833
Reference: parity = 1				
Farm F	0.998	0.158	0.682	1.314
Farm H	1.25	0.157	0.936	1.564
Farm M	0.226	0.168	−0.110	0.562
Farm R	0.989	0.147	0.695	1.283
Farm T	−0.001	0.118	−0.237	0.235
Reference: farm C				
Summer calving	−0.089	0.118	−0.325	0.147
Autumn calving	−0.466	0.116	−0.698	−0.234
Winter calving	−0.593	0.120	−0.833	−0.353
Reference: spring calving				
BCS at DO	0.364	0.095	0.174	0.554
BCS at calving	−0.174	0.099	−0.372	0.024
Dry period length	0.009	0.002	0.005	0.013
Last milk yield (24 h before DO)	0.016	0.006	0.004	0.028
lnSCC in first month before DO	0.023	0.049	−0.075	0.121
lnSCC in second month before DO	0.213	0.045	0.123	0.303
lnSCC in third month before DO	0.172	0.035	0.102	0.242

[1]H- = high SCC category at DO. SQLT2 = selective quarter level treatment antibiotic when CMT (California Mastitis Test) positive, showing at least a weak positive (CMT score ≥2). SQLT1 = selective quarter level antibiotic treatment when CMT positive, showing at least a trace (CMT score ≥1).

treatment programs at the quarter level, when the number of samples to define infection status is quadrupled compared with the cow level. Although on-farm culture was recently also suggested as a way to determine infection status at the quarter level (Kabera et al., 2020), for the reasons indicated above, we used the CMT because it is a fast, easy, and cheap test (Rindsig et al., 1979; Dingwell et al., 2003). In addition to the test, quarter level treatment of only those cows categorized as high SCC at DO, as this study is suggesting, does not require much extra financial nor time investment because, in low SCC herds, the proportion of infected and AB-treated cows at DO is usually less than 25% (Vilar et al., 2018).

If barriers for DO at quarter level are overcome, our study shows AB use at DO can be substantially reduced by a range of 11 to 57% in study herds. This reduction would be on top of antibiotic reductions of 21% (Cameron et al., 2014) and 55% (Rowe et al., 2020a) as shown by others to already be achieved by switching from blanket to selective dry cow treatment at the cow level. Such approaches are in line with recommendations of prudent AB use coming from a growing concern regarding the potential for AB use in food animals to promote the future emergence of antimicrobial resistance in bacteria (O'Neill, 2014). It should be noted this potential AB reduction through DO off at quarter level can only be achieved on well-managed low BMSCC farms with the associated underlying mastitis pathogen etiology as identified in this study, using a teat seal in all quarters, with farmers having the right attitude (Scherpenzeel et al., 2016) and under the careful guidance and monitoring of a capable veterinarian. This all suggests that if cows and udder health are managed well, few AB are needed at DO.

Inadequate sensitivity and specificity of tests to detect infection status at DO has been proposed as a reason for the detrimental effect on udder health of some reported selective dry cow treatment programs (Patel et al., 2017). Indeed, CMT has been shown to not be sensitive enough for use as a screening test for IMI in high SCC herds (Middleton et al., 2004). Also, the positive predictive value of CMT in herds with a bulk tank between 300,000 and 400,000 cells/mL was low;

Table 11. Summary of the final random effects logistical regression model relating to the effect of treatment group on the individual cow SCC at the first DHI test in lactation in cows categorized as low SCC at drying off (DO), from a study in the United Kingdom, comparing selective dry cow treatment at cow level to selective dry cow treatment at quarter level in dairy cows

Covariate[1]	Coefficient	SE	CI Lower	CI Upper
Intercept	0.856			
Treatment group				
AB treatment based on CMT ≥2 (L-SQLT2)	−0.166	0.085	−0.336	0.004
AB treatment based on CMT ≥1 (L-SQLT1)	−0.467	0.086	−0.639	−0.295
Reference: cow level treatment (L-SCLT; sealant only)				
Parity 2	0.073	0.088	−0.103	0.249
Parity 3	0.257	0.122	0.013	0.501
Parity ≥ 4	0.537	0.119	0.299	0.775
Reference: parity = 1				
Farm F	0.955	0.140	0.675	1.235
Farm H	1.943	0.154	1.635	2.251
Farm M	1.729	0.171	1.387	2.071
Farm R	1.103	0.139	0.825	1.381
Farm T	1.013	0.102	0.809	1.217
Reference: farm C				
Summer calving	0.090	0.103	−0.116	0.296
Autumn calving	−0.136	0.104	−0.344	0.072
Winter calving	−0.430	0.102	−0.634	−0.226
Reference: spring calving				
BCS at DO	0.328	0.093	0.142	0.514
BCS at calving	−0.190	0.103	−0.396	0.016
Dry period length	0.002	0.002	−0.002	0.006
Last milk yield (24 h before DO)	0.023	0.007	0.009	0.037
lnSCC in first month before DO	0.125	0.063	−0.001	0.251
lnSCC in second month before DO	0.006	0.069	−0.132	0.144
lnSCC in third month before DO	0.230	0.062	0.106	0.354

[1]L- = low SCC category at DO. SQLT2 = selective quarter level treatment antibiotic when CMT (California Mastitis Test) positive, showing at least a weak positive (CMT score ≥2). SQLT1 = selective quarter level antibiotic treatment when CMT positive, showing at least a trace (CMT score ≥1).

around 40% in late lactation samples (Godden et al., 2017). But in herds, such as in this study, where major pathogen prevalence is low (<10%), CMT seems an acceptable test at DO because the negative predictive value, or the proportion of test-negative animals that are truly negative, can be >95% (Sanford et al., 2006). This means that in low SCC herds, a very small proportion (1 − negative predictive value = less than 5%) of truly infected cows (with major pathogens) would not receive AB dry cow treatment, which is ultimately the goal of a selective dry cow treatment program. Our study showed around 70% of quarters in the high SCC cow category had a positive CMT, and around 70% of quarters in the low SCC category had a negative CMT, suggesting that CMT at the quarter level is not a perfect, but an acceptable test to determine infection status for quarters at DO. This is in line with the findings of Godden et al. (2017) that quarter level CMT tests demonstrated fair to good sensitivity and specificity in late lactation quarters, depending on the cut-off threshold score selected. However, interpreting a CMT test outcome can be subjective. Although we tried to reduce subjectivity by using a trained experienced technician or veterinarian for all cows, untrained farmers themselves would be performing the test in the field. The sensitivity of IMI detection by CMT performed by farmers has been shown to be low (Wallace et al., 2004). Thus, when SQLT is installed using CMT to detect infection status at quarter level, it will be important to train motivated farmers to correctly and uniformly interpret CMT results.

In this study a teat seal was used in all quarters in all cows. This was done because the evidence of teat seal efficacy for the prevention of new infections during the dry period is abundant (Berry and Hillerton, 2002a; Huxley et al., 2002; Krömker et al., 2014), and as a result, has become common practice in most herds in the United Kingdom. However, DO with teat seal is currently not a standard practice everywhere and if teat seal is left out of a selective dry cow treatment approach, low SCC cows at DO may go unprotected for new infections, which, in addition to lack of proper management practices at the herd level (Green et al., 2007), may have been a cause of an increased risk for new IMI as reported in earlier studies (Berry and Hillerton, 2002b; Rabiee and Lean, 2013; Scherpenzeel et al., 2014). Also, the use of teat seal in all quarters was not considered in studies looking at quarter interdependence; it may have increased the independence of quarters during the dry period in this study, suggesting that the application of teat seal in all cows has greatly contributed to the favorable outcome of selective quarter level compared with selective cow level dry cow treatment.

Antibiotic treatment at DO seemed to be very effective because high cure rates were achieved, being consistently above 85%. However, we did not compare AB efficacy to a negative control (no treatment), but compared combined use with a teat sealant to a teat sealant alone which tends to overestimate AB cure rates, likely explaining the high major pathogen apparent cure rates being consistently above 85%, as was also reported in earlier studies (Bradley et al., 2010; Kiesner et al., 2016; Vasquez et al., 2018). In the low SCC cow category at DO, where cow level treatment did not receive any AB at all, apparent self-cure rates were approaching 100%, meaning new infection accounts for the majority of infections present at calving. These high self-cure rates in low SCC cows at DO supports the argument that there is no added value for superimposing AB treatment on a teat sealant in this category of cows.

In this paper we chose to group the non-*aureus Staphylococcus* (**NAS**) spp. together and treated them as a single group. While there is an increasing body of evidence to suggest that all NAS are not equal (Valckenier et al., 2020; Wuytack et al., 2020), we took this approach to facilitate comparison with earlier research in the area. A more detailed analysis of the outcomes and potential roles of the individual NAS spp. would be a fruitful area of future research.

While this research has identified a potential route to further reducing AB use, it has also revealed areas in need of further research. There are clear differences in outcome between herds and cows, suggesting that further investigation of cow and herd level factors affecting dry period outcome could provide useful insights into more appropriate management. Furthermore, because any reduction in the proportion of quarters treated with antibiotic is welcome, a better understanding of how this might affect antimicrobial resistance when there is no effect on the proportion of cows treated within a herd warrants further investigation.

CONCLUSIONS

Our findings suggest that on well-managed low SCC farms, with a low prevalence of major pathogens and a predominant environmental mastitis etiology, selective DO at quarter level using CMT could be a useful approach to further support reduction in antimicrobial use. This approach can be recommended in high SCC cows at DO as a substantial reduction in AB use can be achieved with only minor consequences for udder health. However, in such herds, the superimposition of AB to a teat sealant on high SCC quarters in low SCC cows is not necessary and is unlikely to result in significant gains in udder health.

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