Negatively controlled trial investigating the effects of dry cow therapy on clinical mastitis and culling in multiparous cows

Monika Dziuba,1,2 Luciano S. Caixeta,3 © Brett Boyum,2 Sandra Godden,3 © Erin Royster,3 © and Sam Rowe1 ©
1College of Veterinary Medicine, Michigan State University, East Lansing, MI 48824
2Riverview LLP, Morris, MN 56267
3Department of Veterinary Population Medicine, University of Minnesota, Saint Paul, MN 55108
4Sydney School of Veterinary Science, The University of Sydney, Camden, New South Wales 2570, Australia

ABSTRACT

Blanket dry cow therapy (DCT) is a major contributor to overall antibiotic usage on dairy farms in the United States. With low prevalence of intramammary infections at dry-off in US herds today, alternative DCT approaches have been the focus of much research. We hypothesized that complete cessation of DCT [i.e., use of internal teat sealants (ITS) only at dry-off] could be a practical alternative to blanket DCT in well-managed herds. The objective of this negatively controlled clinical trial was to determine the effects of DCT on clinical mastitis (CM) and removal from the herd during the dry period and the first 200 d of the subsequent lactation in multiparous dairy cows treated with only ITS at dry-off. As a secondary objective, we conducted exploratory analysis to identify subpopulations in the herd (based on parity, previous CM history, and dry-period length) where DCT would not affect postcalving udder health, to generate hypotheses about potential alternative selective DCT programs. The study was conducted in a commercial dairy herd in South Dakota from June 2020 to January 2021. Dry-off sessions (n = 43) were scheduled such that all cows at a given session were dried off using ITS alone (ITS only, n = 20 sessions, n = 1,108 cows) or an intramammary DCT product containing 500 mg of cloxacillin (Dry-Clox, Boehringer Ingelheim) followed by ITS (ITS+ABX, n = 23 sessions, n = 1,331 cows). Culling and CM events were recorded by farm workers who were blinded to the treatment status of cows. Hazard ratios (HR) for the effects of the treatment group on CM and removal from the herd were estimated using multivariable Cox proportional hazards, adjusting for the clustered treatment allocation strategy. Risk of removal from the herd during the dry period was lower in ITS+ABX than ITS-only cows (1.1 vs. 2.7%; HR = 0.45; 95% CI: 0.25 to 0.81). Risk of removal from the herd during the first 200 d of lactation was similar in ITS+ABX and ITS-only cows (17.3 vs. 18.0%; HR = 0.98; 95% CI: 0.82 to 1.18). Risk of CM during the first 200 d of lactation was lower in ITS+ABX cows (6.9%; HR = 0.56; 95% CI: 0.41 to 0.76) compared with ITS-only cows (13.4%). The beneficial effects of DCT on CM and removal from the herd were consistently observed across strata of parity, previous CM history, and dry-period length, indicating that no subpopulations could be identified to withhold DCT. The findings from this study indicate that the omission of DCT from the dry-off procedure, when udder health is not taken into consideration, in multiparous cows can have a negative effect on cow health and welfare. Findings from previous research suggest that culture- or algorithm-guided selective dry cow therapy are likely to be safer approaches to improving antibiotic stewardship. 

Key words: dry cow therapy, mastitis, selective dry cow therapy

INTRODUCTION

Intramammary infection risk during the dry period is higher than at other phases of the lactation cycle (Bradley and Green, 2004) due to increased risk of exposure and decreased resistive capacity to pathogens. It has been shown across multiple studies that the development or persistence of IMI during the dry period leads to increased clinical mastitis (CM) during the following lactation (Green et al., 2002; Rowe et al., 2021a). Therefore, the administration of intramammary antibiotic treatments at dry-off to control dry-period IMI has become a routine practice on commercial dairy farms. The most common strategy for implementing dry cow therapy (DCT) on North American farms is blanket DCT (BDCT), in which all animals and quarters receive antibiotic treatment regardless of infection status (NAHMS, 2014b).
DCT approach has likely contributed to decreased prevalence of contagious mastitis-causing pathogens in herds overall (Bradley, 2002; Ruegg, 2017) but is also one of the main contributors to total antibiotic use in dairy cattle in US herds (de Campos et al., 2021). Recent studies have determined that the quarter-level prevalence of IMI at dry-off in the United States is likely less than 30% (Rowe et al., 2019, 2020a), indicating that most quarters are unlikely to benefit from this antibiotic treatment.

Therefore, to reduce antibiotic usage, alternative DCT strategies are being adopted by farms in the United States, such as selective DCT (SDCT) or complete cessation of DCT. Selective DCT uses screening tools, such as rapid-culture systems or predictive algorithms, to determine which animals and quarters are most likely to benefit from DCT. Studies have found that SDCT can reduce quarter-level antibiotic use by 21 to 58% without negatively affecting udder health (Cameron et al., 2014; Rowe et al., 2020a,b). The recent success of SDCT protocols in clinical trials raises the possibility that well-managed herds (low prevalence of IMI at dry-off and risk during the dry period) may not require DCT at all. However, this hypothesis is inconsistent with findings from a meta-analysis of clinical trials, which found that use of DCT increased the clearance of IMI by 78% and reduced the establishment of new IMI during the dry period by 45% (Halasa et al., 2009a,b). Furthermore, one small clinical trial found that the use of DCT reduced postcalving CM incidence (Cummins and McCaskey, 1987). However, the aforementioned clinical trials were conducted in herds with worse udder health than modern, well-managed farms.

The objective of this negatively controlled clinical trial was to determine the effects of DCT on CM and removal from the herd during the dry period and the first 200 d of the subsequent lactation in multiparous dairy cows. As a secondary objective, we conducted exploratory analysis to identify subpopulations in the herd (e.g., certain parity groups, previous CM history) whose postcalving udder health were not affected by the use of DCT, to generate hypotheses about potential alternative SDCT protocols. We hypothesized that DCT was not necessary in well-managed herds and that the use of internal teat sealants (ITS) alone would be sufficient to maintain cow udder health and welfare after dry-off.

**MATERIALS AND METHODS**

The University of Minnesota Institutional Animal Care and Use Committee approved all procedures for animal handling and care (2002–37913A).

**Study Herd**

The study was conducted in a commercial dairy herd in South Dakota from June 2020 to January 2021. At the time of the study, the lactating herd size was 17,988 cows, which were milked at multiple sites (lactation 1 or greater). All cows were housed in freestall cross-ventilated barns in group pens with deep recycled-sand bedding. Cows calved in designated maternity pens with straw bedding. All enrolled cows were multiparous Jersey-Holstein crossbreeds. The herd had an average bulk milk SCC of 111,000 cells/mL during the time of the study and used a commercial *Escherichia coli* mastitis vaccine (J-VAC, Boehringer Ingelheim). Milk cultures for 65 CM cases during the study period found that *Staphylococcus aureus* and *Streptococcus agalactiae* (i.e., pathogens traditionally targeted using BDCT) were uncommon causes of CM (3 and 0% of cases, respectively). A full table of culture results can be found in supplementary material (Supplementary Table S1; https://osf.io/3qewf/?view_only=29d53ef4f0c8483c9703ae8284d3ae4; Rowe, 2023). Those samples were collected from cows that were not enrolled in the current study. No milk cultures were performed for cows enrolled in the study at any point.

**Cow Enrollment at Dry-Off**

Dry-off sessions (n = 43) over a 2-mo period were scheduled in advance such that all multiparous cows at a given session were dried off either using an ITS (Orbesal, Zoetis) alone (ITS only, n = 1,104 cows) or a commercial intramammary DCT product containing 500 mg of cloxacinil benzathine (Dry-Clox, Boehringer Ingelheim) followed by ITS (ITS+ABX, n = 1,327 cows). Consequently, this study is best described as a “cluster randomized trial” (Brown et al., 2015); however, it should be noted that cows were allocated systematically, rather than through a true random process. Cows were allocated to treatment groups through systematic allocation, in which a 2-wk schedule was created that alternated between ITS only and ITS+ABX from Monday to Friday. Cows were dried off 40 to 60 d before estimated parturition. Week 1 of the schedule assigned all cows dried off on Monday, Wednesday, and Friday to receive ITS+ABX treatment, and all cows dried off on Tuesday and Thursday received ITS only. This pattern was then reversed for wk 2 of the schedule (all cows dried off on Monday, Wednesday, and Friday received ITS only, and all cows dried off on Tuesday and Thursday received ITS+ABX). This 2-wk schedule was repeated for the duration of the study. Dry-off procedures were conducted by farm workers, with the same staff administering treatments to both groups. Before
DCT administration, each teat end was sanitized with isopropyl alcohol, and intramammary treatments were administered to front teats before back teats.

Animals were followed from enrollment until 200 DIM. After dry-off, animals in both treatment groups were managed the same as they were commingled in the far-off dry-cow pen. Farm workers were blinded to treatment allocation of cows. Individual cow outcome data were recorded on the farm’s data management software (DairyComp 305, Valley Ag Software). Outcomes of interest were CM during the first 200 DIM and removal from the herd (i.e., culling or death events) during the dry period and the first 200 DIM. During lactation, suspected mastitis cases were identified in the milking parlors by employees based on biweekly prestripping and daily visual observation for completeness of milk-out and udder inflammation (swelling, pain, redness). Suspected cases were confirmed at the subsequent milking by visual observation of foremilk.

**Statistical Analysis**

All analyses were conducted in R Statistical Programming Environment (R Core Team, 2018). The analysis log can be found at [https://rpubs.com/samrowe/DCT _MN_2021](https://rpubs.com/samrowe/DCT _MN_2021). Sample size was calculated to detect a relatively small but meaningful increase in CM risk from 5% (ITS+ABX) to 7% (ITS only, α = 0.05, power = 0.80, and loss to follow-up = 5%). Based on these assumptions, we originally aimed to enroll 2,250 cows per group (total = 4,500).

All treatments and events of interest (i.e., dry-off, calving, CM, culling, or death) were recorded by farm workers into herd management software using the previously established protocols of the farm. The following explanatory variables were included in the final data set: treatment group (ITS only vs. ITS+ABX), parity (lactation of enrollment is 2, 3, 4, or 5+), date of dry-off, CM history (no cases in the lactation of enrollment is 2, 3, 4, or 5+), and DIM at dry-off. To facilitate exploratory analyses, dry-period length (continuous variable) was split into 3 equal-sized categories (tertiles), such that each cow was classified as having a relatively short (<45 d), typical (45–50 d), or long (>50 d) dry-period length. The following outcome variables were included in the final data set: CM during the first 200 d of lactation (no cases vs. 1 or more cases), removal during the dry period (yes vs. no), and removal during the first 200 d of lactation (yes vs. no). No imputation methods were used for any variables, as very few data were missing.

Survival analysis was conducted to determine the effects of treatment group on CM during the first 200 d of lactation and removal from the herd during the dry period and in the first 200 d of lactation. Crude risk estimates were calculated by dividing the number of cases by the number of cows at risk. Dry-period removal from the herd was defined as any death or culled event during the dry period. Cows were right censored at removal or at calving. For postcalving outcomes, cows were left censored (excluded) if they had died or been culled before calving and were right censored at 200 DIM or at culling or death event. Kaplan-Meier failure curves (1 – survival) were generated, with the logrank test used to compare between treatment groups. Hazard ratios (HR) were estimated using Cox proportional hazards regression, using a robust sandwich estimator to account for the clustered allocation strategy (i.e., cows clustered within dry-off date; Brown et al., 2015). Parity, DIM at dry-off, CM during the lactation of enrollment, and dry-period length were available for inclusion as covariates into multivariable models for CM and removal during the first 200 DIM, as we hypothesized that these variables could be associated with outcomes and thus cause confounding if they were not balanced between treatment groups.

Exploratory analyses were conducted to identify subpopulations in the herd where DCT had no effect on outcomes. The subpopulations of interest were based on parity, history of CM, and dry-period length. This was done by performing similar models to the main effects models, except that interaction terms were added for the variable of interest. Type-2 P-values were calculated for the interaction term to test the null hypothesis that DCT effect was the same across strata. In addition, stratum-specific HR estimates were extracted from interaction models using the “contrast” function within the emmeans package (Lenth et al., 2020). No adjustments were made to confidence intervals to account for multiple comparisons (Rothman, 1990).

**RESULTS**

**Enrollment**

Cows were enrolled from a total of 43 dry-off sessions (ITS only = 20 sessions and 1,104 cows; ITS+ABX = 23 sessions and 1,327 cows). The number of cows enrolled was substantially less than originally planned due to the COVID-19 pandemic. Treatment groups...
ITS only and ITS+ABX) were balanced at the time of enrollment for age (4.82 and 4.64 years old, respectively), DIM (325 ± 50.3 and 317 ± 48.4), history of CM during the previous lactation (11.7 and 9.3%), and expected dry-period length (47.0 and 46.9 d). Distribution of parity was also similar between treatment groups, with overall 43.2% of animals in parity 2 (39.3 and 46.3%), 20.0% in parity 3 (21.7 and 18.6%), 22.5% in parity 4 (23.9 and 21.3%), and 14.3% in parity 5+ (15.0 and 13.7%). The balance of demographic features between treatment groups indicate that the allocation strategy was unlikely to have caused confounding bias.

**Removal from the Herd During the Dry Period and in the First 200 d of Lactation**

A Kaplan-Meier failure curve showing the cumulative incidence of removal from the herd during the dry period is depicted in Figure 1. Hazard ratio estimates and crude risks (overall and stratum-specific) are shown in Table 1. Crude risk of removal from the herd during the dry period was 55% lower in ITS+ABX cows compared with ITS-only cows (1.1 vs. 2.7%; HR = 0.45; 95% CI: 0.25 to 0.81). For interaction models evaluating the effects of DCT on removal during the dry period, P-values for interaction terms were treatment × parity (P = 0.97) and treatment × CM history (P < 0.001). Despite some variation in stratum-specific HR estimates, all estimates were less than 0.6, indicating that DCT reduced removal during the dry period in all subpopulations of cows evaluated.

**Figure 1.** Kaplan-Meier curve showing the cumulative incidence of removal from the herd (culling or death) during the dry period for cows treated at dry-off with an internal teat sealant alone (ITS) or a combination of an intramammary antibiotic and an internal teat sealant (ITS+ABX). The P-value from a logrank test is shown.

**Table 1.** Estimates (overall and stratum-specific) for the effects of dry cow therapy (DCT) on removal from the herd (death or culling) during the dry period.

<table>
<thead>
<tr>
<th>Strata</th>
<th>Crude risk2</th>
<th>Hazard ratio3 (95% CI)</th>
<th>Type 2 P-value4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall All cows</td>
<td>30/1,104 (2.72)</td>
<td>14/1,327 (1.06)</td>
<td>0.45 (0.25–0.81)</td>
</tr>
<tr>
<td>Stratum-specific5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10/434 (2.3)</td>
<td>5/615 (0.81)</td>
<td>0.37 (0.13–1.11)</td>
</tr>
<tr>
<td>3</td>
<td>6/240 (2.5)</td>
<td>2/247 (0.81)</td>
<td>0.47 (0.1–1.97)</td>
</tr>
<tr>
<td>4</td>
<td>5/264 (1.89)</td>
<td>4/283 (1.41)</td>
<td>0.6 (0.15–2.33)</td>
</tr>
<tr>
<td>5+</td>
<td>9/166 (5.42)</td>
<td>3/182 (1.65)</td>
<td>0.45 (0.15–1.33)</td>
</tr>
<tr>
<td>Clinical mastitis history</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>24/975 (2.46)</td>
<td>14/1,204 (1.16)</td>
<td>0.52 (0.29–0.94)</td>
</tr>
<tr>
<td>Yes</td>
<td>6/129 (4.65)</td>
<td>0/123 (0)</td>
<td>NA6</td>
</tr>
</tbody>
</table>

1Cows were dried off using either internal teat sealants alone (ITS only) or an intramammary DCT product containing 500 mg of cloxacillin (Dry-Clox, Boehringer Ingelheim) followed by ITS (ITS+ABX).

2Values are presented as the proportion, with percent in parentheses.

3Hazard ratio estimates were calculated using Cox proportional hazards regression. Models adjusted for clustering of cows within dry-off date and included the following covariates (possible confounders): DIM at enrollment, parity, clinical mastitis history.

4Type 2 analysis of deviance test used to calculate P-value. The null hypothesis was that effects of DCT on removal from the herd did not vary within strata. For example, the P-value for the dry-period length interaction term was <0.001, which suggests that the null hypothesis may be false, and therefore, the effects of DCT may vary depending on clinical mastitis history.

5Models were run using interaction terms to evaluate if the effects of DCT varied in certain subpopulations of animals (e.g., certain parity groups).

6Model could not estimate hazard ratio due to no cases being observed in the ITS+ABX group.
A Kaplan-Meier failure curve showing the cumulative incidence of removal from the herd during the first 200 d of the subsequent lactation is depicted in Figure 2. Hazard ratio estimates and crude risks (overall and stratum-specific) are shown in Table 2. Crude risk of removal from the herd during the first 200 DIM was similar in ITS+ABX and ITS-only cows (17.3 vs. 18.0%; HR = 0.99; 95% CI: 0.82 to 1.19). For interaction models evaluating the effects of DCT on removal during the first 200 d of lactation, P-values for interaction terms were treatment × parity (P = 0.90), treatment × CM history (P = 0.55), and treatment × dry-period length (P = 0.48). Stratum-specific HR estimates were close to 1 (range 0.86 to 1.21), indicating that the effects of DCT on postcalving removal from the herd was limited and consistent across subpopulations within the herd.

**Effects of Dry Cow Therapy on Clinical Mastitis During the First 200 d of Lactation**

A Kaplan-Meier failure curve showing the cumulative incidence of CM during the first 200 DIM of the subsequent lactation is depicted in Figure 3. Hazard ratio estimates and crude risks (overall and stratum-specific) are shown in Table 3. Crude risk of CM during

**Table 2.** Estimates (overall and stratum-specific) for the effects of dry cow therapy (DCT) on removal from the herd (death or culling) during the first 200 d of lactation.

<table>
<thead>
<tr>
<th>Strata</th>
<th>ITS only</th>
<th>ITS+ABX</th>
<th>Hazard ratio (95% CI)</th>
<th>Type 2 P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>193/1,074 (17.97)</td>
<td>227/1,313 (17.29)</td>
<td>0.99 (0.82–1.19)</td>
<td>0.898</td>
</tr>
<tr>
<td>Stratum-specific</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>52/424 (12.26)</td>
<td>78/610 (12.79)</td>
<td>0.98 (0.7–1.36)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>44/234 (18.8)</td>
<td>49/245 (20)</td>
<td>1.07 (0.68–1.69)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>49/259 (18.92)</td>
<td>47/279 (16.85)</td>
<td>1.06 (0.72–1.56)</td>
<td></td>
</tr>
<tr>
<td>5+</td>
<td>48/157 (30.57)</td>
<td>53/179 (29.61)</td>
<td>0.86 (0.57–1.29)</td>
<td></td>
</tr>
<tr>
<td>Clinical mastitis history</td>
<td></td>
<td></td>
<td></td>
<td>0.55</td>
</tr>
<tr>
<td>No</td>
<td>156/951 (16.4)</td>
<td>194/1,190 (16.3)</td>
<td>1.03 (0.81–1.3)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>37/123 (30.08)</td>
<td>33/123 (26.83)</td>
<td>0.82 (0.45–1.51)</td>
<td></td>
</tr>
<tr>
<td>Dry-period length</td>
<td></td>
<td></td>
<td></td>
<td>0.483</td>
</tr>
<tr>
<td>Shortest 33%</td>
<td>69/355 (19.44)</td>
<td>85/441 (19.27)</td>
<td>1.21 (0.79–1.85)</td>
<td></td>
</tr>
<tr>
<td>Middle 33%</td>
<td>67/358 (18.72)</td>
<td>75/438 (17.12)</td>
<td>0.86 (0.58–1.27)</td>
<td></td>
</tr>
<tr>
<td>Longest 33%</td>
<td>57/361 (15.79)</td>
<td>67/434 (15.44)</td>
<td>0.89 (0.63–1.27)</td>
<td></td>
</tr>
</tbody>
</table>

1Cows were dried off using either internal teat sealants alone (ITS only) or an intramammary DCT product containing 500 mg of cloxacillin (Dry-Clox, Boehringer Ingelheim) followed by ITS (ITS+ABX).
2Values are presented as the proportion, with percent in parentheses.
3Hazard ratio estimates were calculated using Cox proportional hazards regression. Models adjusted for clustering of cows within dry-off date and included the following covariates (possible confounders): DIM at enrollment, parity, clinical mastitis history, dry-period length.
4Type 2 analysis of deviance test used to calculate P-value. The null hypothesis was that effects of DCT on removal from the herd did not vary within strata.
5Models were run using interaction terms to evaluate if the effects of DCT varied in certain subpopulations of animals (e.g., certain parity groups).
the first 200 DIM was reduced by 44% in ITS+ABX cows compared with ITS-only cows (6.9 vs. 13.4%; HR = 0.56; 95% CI: 0.41 to 0.76). For interaction models evaluating the effects of DCT on CM, \( P \)-values for interaction terms were treatment \( \times \) parity (\( P = 0.97 \)), treatment \( \times \) CM history (\( P = 0.55 \)), and treatment \( \times \) dry-period length (\( P = 0.04 \)). Stratum-specific HR estimates were all less than 0.70, indicating that DCT reduced postcalving CM within all evaluated subpopulations of cows.

**DISCUSSION**

The primary objective of this negatively controlled clinical trial was to determine the effects of DCT on CM and removal from the herd during the dry period and the first 200 d of the subsequent lactation. We hypothesized that previous negatively controlled trials were not generalizable to current practices and herd demographics. However, we observed a substantial reduction in CM in the subsequent lactation (HR = 0.56) and culling and death during the dry period (HR = 0.45) in cows treated with DCT. Therefore, our findings are consistent with observations seen in previous studies evaluating the effects of DCT on udder health.

Figure 3. Kaplan-Meier curve showing the cumulative incidence of clinical mastitis over the first 200 d of lactation for cows treated at dry-off with an internal teat sealant alone (ITS) or a combination of an intramammary antibiotic and an internal teat sealant (ITS+ABX). The \( P \)-value from a logrank test is shown.
For example, a negatively controlled trial performed by Cummins and McCaskey (1987) also found that animals that received DCT had a 73.6% reduction in incidence of CM in their subsequent lactation.

The observed DCT-associated reduction in postcalving CM is likely due to increased clearance of IMI during the dry period, which was demonstrated in a meta-analysis of clinical trials conducted between 1930 and 2008 (Halasa et al., 2009a,b). This hypothesis is supported by findings from observational studies demonstrating that dry-period IMI are associated with postcalving CM (Green et al., 2002; Rowe et al., 2021a). It should be noted that our study did not investigate IMI dynamics as an evaluator of udder health. We chose to use CM and culling as our outcomes, as they are representative of the downstream effects of IMI during the dry period and are directly relatable and available to producers. However, the limitation of this approach is that we were unable to identify the underlying mechanism for how DCT reduced postcalving CM and dry-period culling. This study did not use individual cow SCC because it was not available or measured in the herd during the time of the study. This resulted in an evaluation of the effectiveness of easier and less costly applications of SDCT to producers. However, a limitation of this approach is that postcalving SCC data were not compared between treatment groups.

This study also found that the use of DCT reduced culling and death during the dry period. To our knowledge, no negatively controlled trials have been conducted to investigate the effects of DCT on removal from the herd. We speculate that the lower incidence of removal from the herd was due to increased dry-period IMI cures and reduced acquisition of new IMI. Although no observational studies have empirically demonstrated this mechanism, it is generally accepted that dry-period IMI can cause severe cases of CM, which can lead to death or culling. This is supported by observational studies that have demonstrated positive associations between new IMI during the dry period and postcalving incidences of CM (Smith et al., 1985; Bradley and Green, 2000). However, it should be noted that the majority of new IMI acquired during the dry period do not cause dry-period CM. This is supported by findings from a recent study by our research group, which found that the cow-level risk of dry-period CM was 0.4% (Rowe et al., 2020b), despite the fact that 20.1% of quarters acquired a new IMI during that period (Rowe et al., 2020a). A study performed by McDougall and Castle (2021) reported that specific characteristics of cows at dry-off, such as age, milk yield before drying off, and timing during lactation cycle at dry-off, also play a role in the risk of acquiring CM during the dry period when given only ITS. It is plausible that the use of DCT can control IMI that are associated with unhygienic administration of ITS at dry-off. However, it should be noted that administration of DCT for this sole purpose is not a judicious use of antibiotics.

Antibiotic-sparing dry-off practices are growing in popularity among dairy farms. This is due to a greater understanding of antimicrobial resistance, an increased push toward transparency and sustainability from consumers, and producers’ rationalization of an improvement in antibiotic stewardship or reduction in costs associated with daily operation. Although either a selective or no DCT method would result in a reduction of antimicrobial use at dry-off, with the greatest effect being seen in no DCT, this may come at the expense of cow health and welfare when it comes to CM and survivability in the herd (Cummins and McCaskey, 1987). Although we did not perform an economic analysis, omitting DCT could also have negative economic implications when exchanging the cost of antibiotic treatment at dry-off with increased cases of CM and increased removal from the herd (Rollin et al., 2015; Rowe et al., 2021b). In summary, our findings indicate that complete cessation of DCT could be a risk to cow health and survival.

Selective DCT programs use screening tools such as rapid culture or predictive algorithms to identify animals that are at greatest risk for IMI and are most likely to benefit from DCT. Algorithm-guided SDCT approaches that use SCC and CM history have been demonstrated to reduce antibiotic use without negatively affected cow health and survival (Bradley et al., 2010; Vasquez et al., 2018; Rowe et al., 2020a,b). However, many farms in the United States do not conduct regular DHI testing (between 39 and 56% of herds and less than 50% of the cows nationally are enrolled in DHIA; NAHMS, 2014a; Dairy One, 2021), which may be a significant barrier to the adoption of algorithm-guided SDCT in US dairy herds. Consequently, as a secondary objective, we conducted exploratory analysis to identify subpopulations of cows in the herd for which DCT administration did not reduce CM and removal from the herd, such that subpopulations of the herd could be identified to not receive DCT. However, the beneficial effects of DCT (i.e., lower incidences of CM and removal from the herd) were consistently observed across strata of parity, previous CM history, and dry-period length, indicating that no subpopulations of multiparous cows could be identified to withhold DCT. Therefore, it is recommended that producers wishing to conduct algorithm-guided SDCT use protocols that are based on individual cow SCC, which can be determined from DHIA milk testing. An important limitation of this study was that SCC information was not collected on enrolled cows, which prevented us from being able...
to directly compare BDCT and SCC-based algorithm-guided SDCT. However, numerous studies have demonstrated that this approach can be successfully implemented without negatively affecting cow health and production, provided that internal teat sealants are used (Kabera et al., 2021).

For herds that are unwilling or unable to perform DHIA testing, a rapid-culture guided approach may be a realistic option that can be done on-farm or in a local veterinary laboratory.

One major strength of this study was the large number of dry-off sessions (n = 43), which include a total of 2,439 individual cows dry-offs, which is significantly larger than previously published negatively controlled DCT trials and enabled us to perform stratified analyses as part of our secondary objective. Our treatment allocation strategy was applied at the cluster (dry-off session) level, which is in contrast to most DCT trials that are allocated at the cow-level. One potential risk with this allocation strategy is that clusters could differ at baseline, which could cause cluster-level confounding. For example, this could happen if cows from certain dry-off sessions had a higher risk of postcalving CM (e.g., if older cows were dried off on certain days). We minimized the risk of this occurring by alternating treatment groups each dry-off session, enrolling a large number of dry-off sessions (n = 43), and using multivariable models to control for variables hypothesized as potential confounders. Furthermore, we found that treatment groups were balanced, indicating that the risk for confounding was low. Another important consideration for cluster randomized trials is the lack of independence for cows within dry-off sessions. To mitigate this, we used a robust sandwich estimator to adjust SE estimates (Brown et al., 2015).

Another strength of this study is that treatments were administered by farm staff, not study personnel, which makes our findings more representative of what may happen on other commercial farms. The disadvantage of this approach is that more variation may occur in how treatments were administered and how outcomes were assessed. However, it should be noted that dry-off sessions were conducted under the supervision of study investigators, and case definitions for outcomes were based on farm protocols, which are outlined in the Methods section of this report. One important limitation of this study was that it was conducted on a single dairy in South Dakota. Furthermore, only multiparous cows were included. Therefore, we recommend that readers consider this when generalizing our findings to other herds.

Further research into the inclusion of first-lactation animals into this study or collection of individual cow-level data points at dry-off, such as California Mastitis Test or rapid SCC at the cow or quarter level, may be able to reveal populations that are beneficial for implementation into a SDCT program.

CONCLUSIONS

This negatively controlled trial investigated the effects of DCT on CM and removal from the herd during the dry period and the first 200 d of the subsequent lactation and possible identification of subpopulations of cows in the herd where DCT was beneficial. This study found that omission of DCT from the dry-off procedure can have a negative effect on cow health and welfare through increases in CM during the subsequent lactation and removal from the herd during the dry period. We recommend that herds seeking to improve antibiotic stewardship consider culture or algorithm-based SDCT protocols.

ACKNOWLEDGMENTS

The funding and technical support for this project was provided by Riverview LLP (Morris, MN) and by the USDA National Institute of Food and Agriculture (Washington, DC), Federal Formula Funds Hatch project number 1024554 to LSC. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the view of the National Institute of Food and Agriculture or the USDA. The authors have not stated any conflicts of interest. Monika Dziuba contributed to investigation, data curation, and writing—original draft, and visualization. Luciano Caixeta contributed to conceptualization, methodology, resources, and writing—review and editing. Sandra Godden contributed to conceptualization, methodology, and writing—review and editing. Brett Boyum contributed to conceptualization, methodology, resources, and project administration. Sam Rowe contributed to conceptualization, methodology, and writing—review and editing. Erin Royster contributed to conceptualization, methodology, and writing—review and editing.

REFERENCES


ORCIDs

Luciano S. Caixeta https://orcid.org/0000-0001-9577-4989

Sandra Godden https://orcid.org/0000-0002-4438-0039

Erin Royster https://orcid.org/0000-0002-8298-5581

Sam Rowe https://orcid.org/0000-0001-8336-6523