ABSTRACT

The objective of this cross-sectional study was to investigate the relationship between management practices and antimicrobial use in heifer calves on Canadian dairy farms. Questionnaires on calf management practices, herd characteristics, and calf treatment records were administered on 147 dairy farms in 5 provinces during annual farm visits in a multiyear, nationwide research project (Canadian Dairy Network for Antimicrobial Stewardship and Resistance: CaDNetASR). Questions focused on the calf caregiver, calving pen, colostrum management, milk feeding, grouping, bedding management, and age when male calves were sold. Antimicrobial treatment records were collected on each farm from either an electronic herd management system or paper-based records. Newborn heifers born in the last 12 mo were identified retrospectively and followed to 60 d of age, with antimicrobial treatments and dates of sale or death extracted for further analysis. A multivariable linear regression model was developed with the natural log of the number of antimicrobial treatments per calf-year as the dependent variable, and categorized calf management practices and farm characteristics as the independent variables. A complete data set of records on 7,817 calves was retrieved from 74 farms based on completeness of calf records. A total of 2,310 calves were treated at least once with an antimicrobial, and 7,307 individual antimicrobial treatments were recorded. Among the reasons for antimicrobial use, respiratory disease (54%) was most common, followed by diarrhea (20%), presence of a fever (3%), and umbilical disease (2%). Florfenicol (33% of recorded treatments), penicillin (23%), and trimethoprim-sulfamethoxazole (18%) were commonly used, whereas fluoroquinolones (4%), and ceftiofur (1%) were used less commonly. Farms (31%) commonly had 0–1.0 antimicrobial treatments/calf-year (median: 2.2 treatments/calf-year; interquartile range: 0.64–4.63 treatments/calf-year). Defined daily dose (DDD) per calf-year was calculated based on the Canadian bovine standards. Among the 74 farms, florfenicol (1.35 DDD/calf-year) and macrolides (0.73 DDD/calf-year) were used most, whereas ceftiofur (0.008 DDD/calf-year) was the lowest. The final multivariable linear regression model indicated that farms that fed transition milk had fewer than half the number of antimicrobial treatments per calf-year than those who did not feed transition milk. The number of antimicrobial treatments per calf-year in preweaning calves was low on many farms, and there was low use of highly important drugs for human medicine. The effect of feeding transition milk should be investigated regarding potential effects on antimicrobial use and disease prevention. 

Key words: heifer, antibiotic use, treatments, practices, antimicrobial stewardship

INTRODUCTION

Antimicrobial resistance (AMR) is an important concern for human and animal health (O’Neill, 2016; Cummings et al., 2019). Development of resistant bacteria is driven by antimicrobial use (AMU). It is thought that AMU in farm animals contributes to human AMR, due to the relatively large amount of antimicrobials used and the use of the same classes of antimicrobials as in humans (PHAC, 2017). Additionally, the zoonotic transmission of resistant bacteria to humans is known to occur (ECDC et al., 2017; Tang et al., 2017). Although in the dairy industry most AMU in dairy cattle is for udder health, calves are also commonly treated with antimicrobials and possess a higher
proportion of resistant bacteria and multidrug-resistant bacteria compared with older cattle (Cao et al., 2019; Redding et al., 2019; de Campos et al., 2021).

Diarrhea and respiratory diseases are common in calves, and these conditions are frequently treated with antimicrobials. Approximately 1 in 4 calves receives antimicrobial treatment, including 69% of calves with signs of digestive illness and 88% of calves with respiratory illness (Urie et al., 2018). In addition to antimicrobial treatment, calf rearing practices (including housing, and feeding waste milk or medicated milk replacer) are associated with morbidity, AMU, and AMR in preweaning calves (Svensson and Liberg, 2006; Holstege et al., 2018; Springer et al., 2019). These calf management practices are often related to each other, where no single element acts as a risk factor for AMU and AMR. For example, calves treated with antimicrobials within 5 d of sampling had greater odds of having resistant fecal Escherichia coli than nontreated calves, but this difference did not occur when calves were fed milk that included antimicrobials (Berge et al., 2006). Other calf management practices, including calving pen, milk feeding, group housing, and bedding material, are associated with calf morbidity and mortality (Medrano-Galarza et al., 2018; Renaud et al., 2018; Karle et al., 2019). Good management practices for feeding colostrum may reduce the number of calves with diarrhea and respiratory disease, improve calf growth, and reduce AMU (Chamorro et al., 2017; Kargar et al., 2020; Cantor et al., 2021). However, the details of AMU in calves and the association between AMU and calf management practices remain unclear in Canadian dairy farms.

The objectives of this study were to (1) describe and quantify antimicrobial use and (2) identify associations between calf management practices and AMU in dairy heifer calves on Canadian dairy farms. We hypothesized that producers with excellent colostrum management practices would have fewer antimicrobial treatments on their farms.

**MATERIALS AND METHODS**

A cross-sectional study was conducted in which survey responses and treatment records were collected during the 2021 annual farm visits of a 5-yr project. This study was part of the Canadian Dairy Network for Antimicrobial Stewardship and Resistance (CaDNetASR) research project, which started in 2019 and was further described by Fonseca et al. (2022). A sample size calculation was conducted, assuming that 95% of farms used between 0.001 and 4 animal-defined doses/1,000 cows of antimicrobials with a precision of 0.3 (Fonseca et al., 2022). In short, 30 dairy farms were enrolled from each of the 5 Canadian provinces. Producers participated in the proAction Initiative (national quality assurance program; Dairy Farmers of Canada, 2021) and had to be raising their own replacement heifers (Fonseca et al., 2022). Dairy producers were recruited by researchers and through local veterinary clinics and are a convenience sample of eligible herds. The study was approved by the University of Guelph (no. 19-04-005) and the University of Prince Edward Island (file no. 6008059) Research Ethics Boards. The manuscript was reported using the STROBE-Vet reporting guideline (O’Connor et al., 2016).

**Questionnaire**

A total of 147 farms (British Columbia: 29; Alberta: 30; Ontario: 35; Québec: 30; Nova Scotia: 23) were visited once between July 5, 2021, and November 26, 2021. Researchers visited the farms and distributed a questionnaire on calf management, which is presented in Supplemental Figure S1 (https://doi.org/10.5683/SP3/9A1PPI; Uyama et al., 2022). The questionnaire was composed of multiple-choice questions and open questions about calf caregiver, calving pen, colostrum feeding, group housing, and sale age of male calves. In the questionnaire, transition milk was defined as the milk obtained from second to sixth milkings after calving. Waste milk was defined as the milk that has been harvested from cows treated with antimicrobials and not having completed their milk withdrawal period. The questionnaire was developed through discussion among multiple research team members. Pilot testing of the questionnaire was not conducted. The questionnaire lasted approximately 15 min and was administered by regional field workers and answered by the producers during the annual CaDNetASR visits. All responses were checked and analyzed by a single researcher (TU). Missing or unclear responses were followed up with farmers by the regional field workers. Responses given for male calves or post-weaning heifers were not analyzed except for the question on sale age of male calves. Multiple answers were allowed for management styles depending on season, age of the calf, or housing style. When multiple responses were selected in multiple-choice questions, all responses were included and presented as the proportion of responses for each category. Thus, the sum of each category may exceed 100%. When a range was given, the mean value was calculated and included in the analysis.

**Treatment Records**

Data on the monthly number of newborn calves, removal of these calves from the farm, and their an-
timicrobial treatments were collected from each farm. Calf ID, sex, and date of birth of newborn calves were collected from each farm. Only newborn heifer calves were followed, and their date of removal from the farm and the reason for removal were captured if the calf died or was sold ≤60 d of age. Information on antimicrobial treatments was collected from the same set of newborn heifer calves ≤60 d of age including the date of treatment, the type of antimicrobial, dose, reason for treatment, and the duration of treatment when indicated. The data were recorded using an electronic herd management system, paper-based records, or a combination of both. When calf treatments were recorded in multiple places, all of them were captured and checked for duplication to remove redundant information. Electronic herd management systems included DairyComp (VAS), DelProTM (DeLaval), DairyPlan C21 (GEA Farm Technologies), T4C (Lely), Lac-T (Lactanet), and DSA (DSAHR). Guidance on extracting data was developed for each system before farm visits and distributed to the researchers. Pictures were taken of paper-based records, including logbooks and DHI calendars.

All data were transferred to Microsoft Excel spreadsheets and checked by a single researcher (TU). Treatment records were not checked in duplicate by another person due to lack of resources. All heifer calves born during the 12 mo before the farm visit were followed to 60 d of age or until death or removal from the farm ≤60 d. Male calves and calves identified as beef were excluded from the analysis, as were calves with unidentifiable or duplicate identification.

Farms with a complete set of data and those with at least one antimicrobial treatment in calves at any age were included in the analysis. Farms (n = 73) were excluded as presented in Figure 1. Reasons for exclusion included farms having a poorly functioning computer, producers using an electronic system other than the ones listed, and those that did not indicate where the antimicrobial treatments in calves were recorded on farm. In addition, 10 farms had treatment records on the farm, but no antimicrobial treatment records could be identified for any calves after scrutinizing the data set. These farms were excluded from the analysis because it was not clear whether the producers recorded no antimicrobial treatments in calves, whether no calves were treated with antimicrobials in this period, or whether those data were recorded elsewhere but were not provided.

Records on nonantimicrobial drugs including halofuginone, anti-bloat drugs, coccidiostats, nonsteroidal anti-inflammatory drugs, glucocorticoids, xylazine, lidocaine, kaolin-pectin, vitamins, insecticides, vaccines, selenium, hormones, bismuth subsalicylate, charcoal, and electrolytes were excluded. Treatments with missing dates, unclear records for treatment, and any treatments recorded before the date of birth or after the date of death were excluded from the included farms. When calves died or were sold up to or before 60 d of age, date and reason of removal were extracted to calculate the number of animal-days at risk on farm. Animal-days at risk was defined as the number of days from birth to 60 d or until the day when a calf was removed from the farm (Earley et al., 2019). When the reason for removal was not clear, calves with treatment records were assumed to have died. Calves with no treatment records or records indicated “abattoir” were assumed to have been sold.
Number of Antimicrobial Treatments per Calf-Year and Defined Daily Dose per Calf-Year

The total number of antimicrobial treatments, the number of days at risk, and the number of antimicrobial treatments per calf-year at the herd level were calculated for each farm. The total number of antimicrobial treatments considered all antimicrobial treatments, including multiple treatments on the same day. The proportion of each antimicrobial class was analyzed among the total antimicrobial treatment records and categorized based on the importance to human health in Canadian standards (Government of Canada, 2009). Furthermore, the number of defined daily doses (DDD) for each antimicrobial type was calculated for each farm as described below. Total mass of antimicrobials used on each farm was calculated by using the antimicrobial concentration on the product label multiplied by volume of product administered to all calves. Information on dose was retrieved from treatment records (recorded for 45.4% of all treatments) or was estimated by calculating the volume to administer to an average sized preweaning calf weighing 64 kg (Jones and Heinrichs, 2020; de Campos et al., 2021). The total mass of antimicrobials was divided by the Canadian defined daily doses (DDDbovCA), which were defined as grams of antimicrobials per animal per day (Lardé et al., 2020). The combination of antimicrobials was calculated separately for each antimicrobial except for trimethoprim-sulfamethoxazole (Lardé et al., 2020). Long-acting antimicrobials were treated similarly to other antimicrobials because they were applied to calves in shorter intervals on the included farms. The number of DDD per calf year was calculated as follows:

\[
\text{DDD per calf year} = \frac{\text{Total mass of antimicrobial (mg)} \times 365 \text{ d}}{\text{DDDbovCA} \left( \frac{\text{g}}{\text{animal per d}} \right) \times 1,000 \times \text{number of animal-days at risk on farm}}
\]

Statistical Analysis

A multivariable linear regression model was developed using the log-transformation of the number of antimicrobial treatments per calf-year as the dependent variable. Calf management practices (i.e., calf caregiver, calving pen, colostrum management, milk feeding, grouping, bedding, and sale age of male calves), province, and herd size served as independent variables. The dependent variable was log-transformed because the data were not normally distributed. The association between mortality and the number of antimicrobial treatments per calf-year was also analyzed. Mortality was defined as the proportion of calves that died ≤ 60 d of age among the newborn heifers and was categorized into low (0%), medium (<6%), and high (≥6%) based on the Canadian recommendation on calf mortality (Winder et al., 2018; DFC and NFACC, 2021). Questionnaire responses were categorized to serve as potential independent variables. When multiple answers were selected for multiple-choice questions (i.e., group size, group age range, and frequency of adding and removal of bedding), the largest group size, the widest age range, and the lowest frequency of bedding were selected. Herd size was the number of milking cows on the day of the farm visit. Herd size had a nonlinear relationship with AMU in a locally weighted smoothing curve and was categorized into small (45–86 milking cows), medium (87–166 milking cows), or large (167–475 milking cows) farms based on the 2 average herd sizes in western and eastern Canadian provinces (Progressive Dairy, 2020).

RESULTS

Questionnaire

Demographic Information. Distribution of the responses to the questionnaire are presented in
The median number of milking cows was 111 (range: 34–625). The farm owner was commonly the primary calf caregiver (39.5%; 58/147) and decided when to use antimicrobials on calves (49.7%; 73/147). Most farms (87.8%; 129/147) had a calving pen, but more than half (53.1%; 78/147) used pens for other purposes, including keeping sick cows. Average time of moving calves from the calving area to a calf housing facility varied among farms, with many producers (40.1%; 59/147) moving calves 30 min to 3 h after calving, and few producers (9.5%; 14/147) moving calves within 30 min after calving.

**Colostrum Management.** Colostrum was harvested at a wide range of times after calving. Many producers (30.3%; 44/145) harvested colostrum at 2 to 3 h after calving, but a few (20.0%; 29/145) harvested colostrum >5 h after calving. Most producers (86.4%; 127/147) hand-fed fresh colostrum to calves, followed by frozen colostrum (37.4%; 55/147), and colostrum replacer (35.4%; 52/147). However, among producers who hand-fed fresh colostrum, the proportion of the last 10 calves fed with this type of colostrum ranged from 10 to 100% (median: 90%). Similarly, the range of calves fed with other types of colostrum varied greatly (Figure 2). Time of feeding colostrum for the first time after birth ranged from immediately after birth to 12 h after birth (median: 2.5 h). The volume of colostrum fed at first feeding ranged from 0.5 L to 6 L (median: 3 L). Two farms were unable to provide the timing or volume of the first feeding of colostrum due to allowing the calf to suckle the dam for colostrum intake. Half of producers checked the quality of colostrum with a digital Brix refractometer (26.5%; 39/147), an optical Brix refractometer (21.1%; 31/147), or a colostrometer (2.0%; 3/147). The cut-off values of Brix percentage ranged from 16 to 27% (median: 22%), with more than half (51.4%; 36/70) of producers who used Brix refractometers using a threshold of 22%. One-third of producers (33.3%; 49/147) checked calves for transfer of passive immunity in the last 12 mo. Many producers (70.1%; 103/147) also fed transition milk to calves, with more than half of them feeding transition milk for 2 to 3 d after birth, with 6 to 8 L/d being the average amount fed.

**Nutrition.** Many producers (64.6%; 95/147) fed milk replacer, followed by saleable milk or whole milk (29.9%; 44/147), waste milk (19.7%; 29/147), and other types of milk (11.6%; 17/147). However, the proportion of calves fed with each type of milk per farm varied [milk replacer (range: 10–100% of calves; median: 100%), salable milk or whole milk (range: 7–100%; median: 100%), and waste milk (3–100%; median: 30%)]. Seventeen producers fed other types of milk, including milk with high SCC or a mix of high-SCC milk with other types of milk (n = 13). Half of producers (50.3%; 74/147) fed a maximum amount of ≥9 L or ad libitum milk per day, followed by 8 L/d (27.2%; 40/147) and 6 L/d (11.6%; 17/147).

**Housing.** Half of producers kept calves individually (49.0%; 72/147), and the others kept calves in groups (12.9%; 19/147) or used both individual and group
housing (38.1%; 56/147). For those that used group housing, calves were commonly put into groups at 1 wk old (60.0%; 45/75), in groups of 3 to 6 calves (48.0%; 36/75), with the range in ages of calves in each group being 3 to 4 wk (46.7%; 35/75). More than half of the farms used straw (68.7%; 101/147) or sawdust (63.9%; 94/147) as bedding material. Most producers (76.9%; 113/147) added bedding at least twice per week, and most (63.9%; 94/147) producers removed bedding less than once per month. Almost half of producers (43.8%; 64/146) sold their male calves at 4–7 d, followed by 8–14 d (36.3%; 53/146), >14 d (15.1%; 22/146), or 1–3 d (6.2%; 9/146). Only 1 farm did not sell their male calves.

**Treatment Records**

**General Antimicrobial Use.** Among the 147 enrolled farms, only 74 farms had complete data sets that were suitable for analysis (British Columbia: 13; Alberta: 16; Ontario: 25; Québec: 12; Nova Scotia: 8). A total of 7,817 calves were included in the analysis, with 2,310 calves (29.6%) treated at least once with antimicrobials. The proportion of calves treated with antimicrobials on farms ranged from 0 to 88% (median: 20%). A total of 7,307 antimicrobial treatment records were retrieved for heifer calves 0 to 60 d old. The median number of heifers born in the 12-mo period evaluated was 75 calves per farm (range: 7 to 357) with a median total of 29 antimicrobial treatments (range: 0 to 1,110) administered to calves over 1 yr. Most antimicrobial treatments (n = 3,925; 53.7%) were related to respiratory diseases, followed by diarrhea (n = 1,467; 20.1%), fever (n = 200; 2.7%), navel problem (n = 125; 1.7%), joint inflammation (n = 66; 0.9%), ear infection (n = 53; 0.7%), abscess (n = 37; 0.5%), eye infection (n = 28; 0.4%), injuries (n = 11; 0.2%), and other health related issues (n = 9; 0.1%). Some records (n = 1,386; 19.0%) did not indicate the reason for treatment. Most farms (31%) used 0 to 1.0 antimicrobial treatments/calf-year, followed by 18% using 1.1 to 2.0 antimicrobial treatments/calf-year (median: 2.2 treatments/calf-year; range: 0–32.6 treatments/calf-year; Figure 3).

**Mortality.** Among the 7,817 calves, 361 (4.6%) died during the study period (range of age at death: 0–60 d; median: 14 d). Most farms (73.0%; 54/74) had a herd-level mortality risk of less than 6%. We observed no association between mortality risk and the number of antimicrobial treatments per calf-year (Table 1).

**Number of Antimicrobial Treatments per Calf-Year.** Treatments were categorized into each antimicrobial class, with amphenicols (32.7% of recorded treatments) and β-lactams (penicillin: 22.6%; cefotiofur: 1.1%) used most frequently, followed by macrolides.
Table 1. Univariable association between the natural log of antimicrobial treatments per calf-year and calf management practices (n = 74)

| Item                                                                 | Coefficient | P-value |
|----------------------------------------------------------------------|-------------|---------|
| Province                                                             |             |         |
| Alberta                                                              | 0.37        | 0.55    |
| British Columbia                                                    | 0.14        | 0.83    |
| Nova Scotia                                                          | -0.64       | 0.39    |
| Ontario                                                             | 0.87        | 0.14    |
| Québec                                                              | Referent    |         |
| Herd size                                                           |             |         |
| Small (45–86 milking cows)                                          | Referent    |         |
| Medium (87–166 milking cows)                                        | 0.61        | 0.19    |
| Large (167–475 milking cows)                                        | 1.45        | 0.003   |
| Primary calf caregiver                                               |             |         |
| Owner                                                                | Referent    |         |
| Designated calf caregiver (single person)                           | 0.74        | 0.16    |
| Other, combination                                                  | 0.54        | 0.24    |
| Person who decides when a calf receives antimicrobial therapy        |             |         |
| Owner                                                                | Referent    |         |
| Designated calf caregiver (single person)                           | 0.94        | 0.06    |
| Other, combination                                                  | 0.94        | 0.03    |
| Calving pen                                                         |             |         |
| No                                                                   | Referent    |         |
| Yes, for other purposes                                             | 0.06        | 0.92    |
| Yes, only for calving                                               | 0.78        | 0.22    |
| Timing of moving calves from the calving area to a calf housing facility |         |         |
| Immediately or within 30 min                                        | Referent    |         |
| 30 min–3 h                                                          | -0.43       | 0.48    |
| >3 h                                                                 | -0.73       | 0.23    |
| Timing of harvesting colostrum from the dam after calving           |             |         |
| <2 h                                                                | Referent    |         |
| 2–3 h                                                               | -0.49       | 0.35    |
| >3 h or unknown                                                     | -0.41       | 0.40    |
| Type of colostrum fed to calves                                    |             |         |
| Hand-fed fresh colostrum most common                                | Referent    |         |
| Hand-fed fresh colostrum equal or less common than other types of colostrum | -0.08 | 0.86 |
| Number of colostrum feedings                                       |             |         |
| Once, twice                                                         | Referent    |         |
| More than twice                                                     | -0.34       | 0.39    |
| Timing of first colostrum feeding after birth                       |             |         |
| <4 h                                                                | Referent    |         |
| ≥4 h                                                                | -0.32       | 0.46    |
| Volume of colostrum at first feeding                                |             |         |
| <3 L                                                                | Referent    |         |
| ≥3 L                                                                | -0.05       | 0.92    |
| Colostrum quality check                                             |             |         |
| No                                                                   | Referent    |         |
| Yes                                                                  | 1.30        | 0.001   |
| Transfer of passive immunity checked in last 12 mo                  |             |         |
| No                                                                   | Referent    |         |
| Yes                                                                  | 0.41        | 0.29    |
| Feed transition milk                                                |             |         |
| No                                                                   | Referent    |         |
| Yes                                                                  | -1.08       | 0.008   |
| Days fed transition milk                                            |             |         |
| No feed or unknown                                                  | Referent    |         |
| 1–3 d                                                               | -0.98       | 0.03    |
| ≥4 d                                                                | -1.21       | 0.01    |
| Amount of transition milk fed per day                               |             |         |
| No feed or unknown                                                  | Referent    |         |
| ≤5 L/d                                                              | -0.58       | 0.26    |
| ≥6 L/d                                                              | -1.32       | 0.002   |
| Type of milk fed to calves                                          |             |         |
| Only milk replacer                                                  | Referent    |         |

Continued
fluoroquinolones (4.2%), aminoglycosides (3.0%), sulfonamides (2.6%), and tetracyclines (2.0%; Figure 4). A combination of antimicrobial classes was used as trimethoprim-sulfamethoxazole (18.0%), neomycin-sulfonamide (2.3%), and lincomycin-spectinomycin (0.1%). Some treatments (1.6%; n = 119) were not possible to classify in antimicrobial categories because 2 different classes of antimicrobials were noted and it was not clear whether both were used or if one of them was used but recorded in error (n = 117), or treatments were recorded by veterinarians elsewhere (n = 2). The number of DDD per calf-year was calculated for each class of antimicrobial per farm. Not all farms used each class of antimicrobials. Treatments with aminoglycosides (n = 219; 1 farm), lincomycin-spectinomycin (n = 10; 1 farm), and oral amoxicillin (n = 4; 1 farm) were not calculated for the number of DDD per calf-year because these products had no assigned Canadian DDDbovCA (Lardé et al., 2020).

**Defined Daily Dose per Calf-Year.** Among all enrolled farms (n = 74), the mean number of DDD per calf-year was highest for florfenicol (mean: 1.35 DDD/calf-year; median: 0.42 DDD/calf-year; range: 0–16 DDD/calf-year), followed by macrolides (mean: 0.73 DDD/calf-year; median: 0 DDD/calf-year; range: 0–10 DDD/calf-year), and the lowest in ceftiofur (mean: 0.008 DDD/calf-year; median: 0 DDD/calf-year; range: 0–0.24 DDD/calf-year; Table 2). Among the farms that used each antimicrobial, the number of DDD per calf-year was highest for macrolides (31 farms using these; median: 1.07 DDD/calf-year; range 0.09–10.04 DDD/

| Item                                                                 | Coefficient | P-value |
|----------------------------------------------------------------------|-------------|---------|
| Salable milk/whole milk/transition milk/combination of either       | 0.42        | 0.38    |
| Waste milk/high SCC milk/combination of either                      | −0.44       | 0.36    |
| Maximum amount of milk fed per day                                  |             |         |
| ≤6 L/d                                                              | Referent    |         |
| 6–8 L/d                                                             | 0.71        | 0.34    |
| ≥9 L/d or ad libitum                                                 | 0.99        | 0.18    |
| Pre/probiotics added to milk                                        |             |         |
| No                                                                  | Referent    |         |
| Yes                                                                 | 0.41        | 0.41    |
| Housing of preweaning calves                                        |             |         |
| Individual                                                          | Referent    | 0.56    |
| Group or both                                                       |             | 0.16    |
| Age of calves put into groups for the first time                    |             |         |
| Individual                                                          | Referent    |         |
| 1 wk                                                                | 0.41        | 0.32    |
| ≥2 wk                                                               | 1.00        | 0.09    |
| Group size                                                          |             |         |
| Individual                                                          | Referent    |         |
| 2–6 calves                                                          | 0.08        | 0.86    |
| ≥7 calves                                                           | 1.09        | 0.02    |
| Range of age of calves in the group                                  |             |         |
| Individual                                                          | Referent    |         |
| ≤2 wk                                                               | 0.31        | 0.56    |
| ≥3 wk                                                               | 0.69        | 0.11    |
| Bedding material                                                     |             |         |
| Straw/hay/combo of either                                           | Referent    |         |
| Other                                                               | −0.71       | 0.11    |
| Add bedding material                                                 |             |         |
| ≥Twice/week                                                          | Referent    |         |
| ≤Once/week                                                          | 0.22        | 0.61    |
| Remove bedding material                                             |             |         |
| ≤Once/month                                                          | Referent    |         |
| >One/month                                                           | −0.61       | 0.13    |
| Bull sale age                                                       |             |         |
| 1–7 d                                                               | Referent    |         |
| 8–14 d                                                              | −0.83       | 0.04    |
| >14 d                                                               | −1.41       | 0.03    |
| Mortality                                                            |             |         |
| 0–6%                                                                | Referent    |         |
| ≥6%                                                                 | 0.84        | 0.07    |
|                                                                      | 0.83        | 0.12    |
calf-year), followed by florfenicol (57 farms; median: 0.99 DDD/calf-year; range: 0.0004–16.33 DDD/calf-year), and the lowest in ceftiofur (8 farms; median: 0.05 DDD/calf-year; range: 0.02–0.24 DDD/calf-year; Table 2).

**Multivariable Analysis.** Chi-squared test for independence was conducted for each explanatory variable between the farms that were included (n = 74) and excluded (n = 73; Supplemental Table S2; https://doi.org/10.5683/SP3/9A1PPI; Uyama et al., 2022). Farms that were included were more likely to check colostrum quality (P = 0.02), evaluate transfer of passive immunity in the last 12 mo (P = 0.01), house calves in groups or a combination of individual and group housing compared with individual housing only (P = 0.04), and had a different distribution of province locations (P = 0.04). However, no significant difference was seen in a pairwise analysis between provinces after Bonferroni’s adjustment.

Among the included farms, province, herd size (small, medium, large), the person who decided antimicrobial therapy for calves (owner, single designated calf caregiver, others), checking colostrum quality (yes, no), feeding transition milk (yes, no), maximum amount of milk fed per day (≤6 L/d, 6–8 L/d, ≥9 L/d or ad libitum), housing type (individual only, group housing, or both), were included in the analysis. The results showed that farms that were included were more likely to check colostrum quality, evaluate transfer of passive immunity in the last 12 mo, house calves in groups or a combination of individual and group housing compared with individual housing only, and had a different distribution of province locations. However, no significant difference was seen in a pairwise analysis between provinces after Bonferroni’s adjustment.

**Figure 4.** Distribution of treatments for antimicrobials used in calves 0 to 60 d of age born in the prior 12 mo on 74 Canadian dairy farms. Antimicrobials are classified from category 1 to 3 based on the importance to human medicine in Canadian standards (Government of Canada, 2009).
or combination of both individual and group housing), bedding material used for preweaning calves (straw or hay, or combination of either, other), frequency of bedding removal (less than once a month, more than once a month), and sale age of the male calves (1–7 d, 8–14 d, >14 d) showed a univariable association with the natural log of antimicrobial treatments per calf-year (Table 1). Province, person who decided antimicrobial therapy for calves, checking colostrum quality, feeding transition milk, frequency of bedding removal, and sale age of the male calves were included in the final model (Table 3). Farms that fed transition milk had fewer than half the number of antimicrobial treatments per calf-year (median: 3.9 treatments/calf-year) compared with those who did not feed transition milk (median: 9.3 treatments/calf-year; Figure 5).

DISCUSSION

In our study, 29.6% of calves were treated at least once with antimicrobials, with 54% of antimicrobial treatments being for respiratory disease and 20% being for diarrhea. Mean herd-level mortality in the preweaning period was 4.6%. Farms (31%) most commonly had 0 to 1.0 antimicrobial treatments/calf-year. These results are similar to a nationwide study in the United States, where 27% of calves received antibiotics and mortality was 5.0% (Urie et al., 2018), whereas in a Canadian study 22 to 23% of calves were treated at least once for disease and 3.5% of calves died (Windeyer et al., 2014). To the best of our knowledge, no other observational study has quantified AMU in Canadian dairy calves.

We found a median of 2.2 antimicrobial treatments/calf-year on a convenience sample of farms, which was calculated by summing the number of antimicrobial treatments divided by the total number of days at risk for heifers born in the last 12 mo for each farm. In a Dutch case-control study, high (>28 DDDA_F; animal daily-defined dose at the farm level) and low within-herd AMU (<0.5 DDDA_F) in calves were defined with DDDA_F as the defined daily dose animal per animal-

Table 3. Final multivariable linear regression on the natural logarithm of the number of antimicrobial treatments per calf-year in relation to calf management practices (n = 74 farms)

| Item                                      | Coefficient | 95% CI       | P-value |
|-------------------------------------------|-------------|--------------|---------|
| Province                                  |             |              |         |
| British Columbia                          | −1.50       | −2.96 to −0.04 | 0.04    |
| Alberta                                   | −1.66       | −3.07 to −0.25 | 0.02    |
| Ontario                                   | −0.57       | −1.81 to 0.67 | 0.36    |
| Québec                                    | Referent    |              |         |
| Nova Scotia                               | −1.73       | −3.10 to −0.36 | 0.01    |
| Antimicrobial therapy decision maker      |             |              |         |
| Owner                                     | Referent    |              |         |
| Designated calf caregiver (single)        | 0.76        | −0.19 to 1.71 | 0.11    |
| Other                                     | 0.44        | −0.40 to 1.29 | 0.30    |
| Colostrum quality check                   |             |              |         |
| Yes                                       | Referent    |              |         |
| No                                        | 1.00        | 0.29 to 1.72  | 0.006   |
| Transition milk                           |             |              |         |
| No                                        | Referent    |              |         |
| Yes                                       | −0.87       | −1.63 to −0.11 | 0.03    |
| Bedding removal frequency                 |             |              |         |
| <Once/month                               | Referent    |              |         |
| ≥Once/month                               | −0.65       | −1.47 to 0.17 | 0.12    |
| Bull sale age                             |             |              |         |
| 1–7 d                                     | Referent    |              |         |
| 8–14 d                                    | −0.97       | −1.86 to −0.08 | 0.03    |
| >14 d                                     | −1.02       | −2.22 to 0.17 | 0.09    |
| Constant                                  | 1.92        | 0.42 to 3.42  | 0.01    |
year (Holstege et al., 2018; SDa, 2021). The DDDA_F was calculated by dividing the total number of treated kilograms of cattle per farm for a specific year with the average number of kilograms of animal present on the farm (SDa, 2021). This study used a data set collected through a national mandatory system and calculated the total DDDA_F which included both oral and parenteral AMU (Holstege et al., 2018). A US study found a median AMU of 19.4 DDD/1,000 animal-days in preweaning calves with injectable antimicrobials (de Campos et al., 2021). The DDD in preweaning calves was defined as the sum of animal-defined doses in preweaning calves divided by the average number of preweaning calves at risk during the 1-yr period (de Campos et al., 2021). We presented 2 AMU metrics: the number of antimicrobial treatments per calf-year and the number of DDD per calf-year in antimicrobials used based on Canadian bovine standards (Lardé et al., 2020) to provide a better description of our data. Different AMU metrics can serve different objectives. Several studies on farm animals have presented multiple AMU metrics (O’Neill et al., 2020; Sanders et al., 2020; de Campos et al., 2021), where the outcome could vary by more than 10-fold (O’Neill et al., 2020). In addition, AMU could be quantified differently depending on AMU collection method (e.g., garbage can audit, veterinary sales, treatment records), study period, methods used to quantify AMU, and standard values used (Nobrega et al., 2017; Redding et al., 2019; Lardé et al., 2021). Farm records underestimated AMU compared with a garbage can audit; farm recorded treatments show moderate (Lardé et al., 2021a) to strong correlations with garbage can audits (Nobrega et al., 2017). No single metric addresses all common questions about AMU.

Among the 7,307 antimicrobial treatment records obtained from 74 farms, florfenicol (33% of treatment records; 1.35 DDD/calf-year) was used most commonly along with penicillin (23% of treatment records; 0.49 DDD/calf-year) and macrolides (9.8% of treatment records; 0.73 DDD/calf-year). Fluoroquinolone (4.2% of treatment records; 0.090 DDD/calf-year) and ceftiofur (1.1% of treatment records; 0.008 DDD/calf-year) were used less commonly. The results of this study were similar to a nationwide study in the United States, where macrolides and florfenicol were most commonly used in respiratory cases (Urie et al., 2018). Other studies have found different results, with a higher usage of fluoroquinolones (8.5 DDD/1,000 animal-days), sulfonamides (5.8 DDD/1,000 animal-days), and penicillin (3.0 DDD/1,000 animal-days), whereas macrolides (2.8 DDD/1,000 animal-days) were used less commonly (Earley et al., 2019). Earley et al. (2019) calculated DDD per 1,000 calf-days for each antimicrobial among the entire farms (i.e., include farms with zero use), and animal-days at risk as the number of days from birth to being removed from the farm, death, or the end of study observation period, which were similar to our study. Another study found that penicillin (5.08 DDD/1,000 calf-days) and enrofloxacin (1.34 DDD/1,000 calf-days) were commonly used, with macrolides (1.24 DDD/1,000 calf-days), and florfenicol (0.51 DDD/1,000 calf-days) used less commonly (de Campos et al., 2021). De Campos et al. (2021) calculated the least squares means of DDD per 1,000 calf-days for each antimicrobial among the farms that used these antimicrobials, and investigated calves under 60 d of life, similarly to our study. The different findings between studies could be attributable to different study populations, morbidity, standardized variables used in calculating AMU, and policies. The World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO), and the World Organisation for Animal Health (WOAH) have developed a global action plan on AMR that lets countries adopt stricter regulations on the prudent use of antimicrobials to tackle AMR (WHO, 2015; Ryan, 2021). For example, Denmark has introduced taxes on certain antimicrobials including fluoroquinolones and third- and fourth-generation cephalosporins (Ryan, 2021). Similarly, the United States prohibited certain extra-label use of third- and fourth-generation cephalosporins in farm animals (FDA, 2021). The European Union is banning any routine use of antimicrobials on farm animals, including the use of medicated feed for prophylaxis (Nunan, 2022). Aligned with the global trend of restricting the use of certain important antimicrobials, usage on our farms of fluoroquinolones and ceftiofur was low, which suggests prudent use of such antimicrobials in Canadian calves (Government of Canada, 2009; McEwen and Collignon, 2018).

We found that farms that did not feed transition milk had more than twice the number of antimicrobial treatments per calf-year than those that fed transition milk to calves. A growing body of evidence highlights the benefits of feeding of colostrum or colostrum replacer beyond the first day of life (Carter et al., 2021). Randomized controlled trials have demonstrated fewer days with diarrhea, lower odds of showing abnormal clinical signs, lower odds of antimicrobial therapy, and increased BW when colostrum or colostrum replacer is fed beyond the first few days of life (Berge et al., 2009; Chamorro et al., 2017; Kargar et al., 2020). When specifically evaluating transition milk feeding, more limited effects of feeding transition milk on calf health have been found. In a randomized controlled trial, 2 or 4 additional feedings of transition milk did not improve cough or fecal scores but improved eye or ear and nasal scores (Conneely et al., 2014). Similarly,
calves fed transition milk 3 times daily between 2 and 4 d of age showed no difference in clinical health scores but increased body weight than those fed with milk replacer (Van Soest et al., 2020). However, when calves were fed 2 L of transition milk with 4 L of pasteurized waste milk for 21 d, they had shorter duration of diarrhea, lower occurrence of diarrhea, and increased withers height during the preweaning period compared with calves fed 6 L of pasteurized waste milk without transition milk for 21 d (Kargar et al., 2021). Transition milk contains lower concentrations of bioactive components than colostrum but higher concentrations than milk, including IgG, growth hormones, and oligosaccharides (Fischer et al., 2019; Godden et al., 2019; Carter et al., 2021). These bioactive components help stabilize the gut microbiota, develop the gastrointestinal tract, inhibit pathogens from attaching to intestinal epithelial cells, and have anti-inflammatory actions (Fischer et al., 2019; Carter et al., 2021). Because feeding transition milk is a common practice on many farms, its potential calf health benefits should be further studied.

One of the limitations of this study was that farms were a convenience sample from 5 provinces, so they might not represent the average Canadian dairy farm. Voluntary bias could be possible because producers with better management practices and possibly less AMU could have been more likely to participate in this study. Furthermore, AMU in calves was calculated from farm treatment records, which may not accurately record the actual use on farms. The results should be interpreted with caution because farm records have been found to underestimate AMU compared with a garbage can audit (Nobrega et al., 2017; Lardé et al., 2021a). An additional limitation is that we did not collect data on in-feed antimicrobials such as medicated milk replacer or medicated premix. Oral administration of antimicrobials could be a common practice in preweaning calves and may play an important role with AMR (Khachatryan et al., 2004; USDA, 2012). Furthermore, almost half of the farms were excluded from multivariable analysis due to incomplete set of data, which could have resulted in a lack of power, and the results should be interpreted cautiously. These farms showed differences in some survey responses compared with those included in the analysis such as checking colostrum quality and transfer of passive immunity status. It could be possible that excluded farms had poorer management practices and different AMU compared with included farms, leading to selection bias. However, we found no difference in the proportion of farms that fed transition milk to calves, which was our key finding, as farms that fed transition milk had lower numbers of antimicrobial treatments per calf-year than those that did not feed transition milk to calves. Previous studies have identified poor record keeping on calves (Waltner-Toews et al., 1986; Lundborg et al., 2005; McGuirk, 2008), which occurred in our study, where more than half of the treatment records did not indicate the dose of antimicrobials applied to calves. However, this was better than a previous finding of >90% of records missing or having incomplete information (Nobrega et al., 2017). Good record keeping of calves on a single, easily accessible herd management system is encouraged, which could aid in monitoring and quantifying morbidity and AMU in calves.

CONCLUSIONS

Preweaning calves were frequently treated with antimicrobials, mostly with antimicrobials that were of moderate to low importance to human medicine and rarely with high priority antimicrobial classes. Feeding transition milk was a common practice, which was associated with lower AMU, but more studies should be performed to validate its effect. Using a standardized electronic herd management system for calves would be greatly beneficial for collection of AMU data to compare within a farm over time and between farms.

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