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Adoption and decision factors regarding selective treatment of clinical mastitis on Canadian dairy farms

Ellen de Jong,[1,2] Kayley D. McCubbin,[1,2] Tamaki Uyama,[3] Carmen Brummelhuis,[4] Julia Bodaneze,[1,2] David F. Kelton,[3] Simon Dufour,[5] Javier Sanchez,[6] Jean-Philippe Roy,[5] Luke C. Heider,[6] Daniella Rizzo,[7] David Léger,[7] and Herman W. Barkema[1,2]*

[1]Faculty of Veterinary Medicine, University of Calgary, Calgary, AB, Canada, T2N 4N1
[2]One Health at UCalgary, University of Calgary, Calgary, AB, Canada, T2N 4N1
[3]Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, ON, Canada, N1G 2W1
[4]Faculty of Veterinary Medicine, Utrecht University, 3584CS Utrecht, the Netherlands
[5]Faculty of Veterinary Medicine, Université de Montréal, Saint-Hyacinthe, Canada, J2S 2M2
[6]Department of Health Management, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PEI, Canada, C1A 4P3
[7]Public Health Agency of Canada, Centre for Foodborne, Environmental and Zoonotic Infectious Diseases, Guelph, ON, Canada, N1H 8J1

ABSTRACT

As clinical mastitis (CM) treatments are responsible for a large portion of antimicrobial use on dairy farms, many selective CM treatment protocols have been developed and evaluated against a blanket treatment approach of CM cases. Selective treatment protocols use outcomes of diagnostic tests to exclude CM cases from antimicrobial treatment when they are unlikely to benefit. To tailor interventions to increase uptake of selective treatment strategies, a comprehension of current on-farm treatment practices and factors affecting treatment decisions is vital. Two questionnaires were conducted among 142 farms across 5 provinces participating in the Canadian Dairy Network for Antimicrobial Stewardship and Resistance in this cross-sectional study. Self-reported adoption of selective CM treatments by dairy farmers was 64%, with median of 82% of cows treated in those herds using selective treatment. Using logistic regression models, the odds to implement a selective CM treatment protocol increased with a decreasing average cow somatic cell count. No other associations were identified between use of a selective CM treatment protocol and farm characteristics (herd size, CM incidence, province, milking system, and housing system). Three subsets of farmers making cow-level CM treatment decisions were identified using a cluster analysis approach: those who based decisions almost exclusively on severity of clinical signs, those who used various udder health indicators, and farmers who also incorporated more general cow information such as production, age, and genetics. When somatic cell count was considered, the median threshold used for treating was >300,000 cells/mL at the last Dairy Herd Improvement test. Various thresholds were present among those considering CM case history. Veterinary laboratories were most frequently used for bacteriological testing. Test results were used to start, change, and stop treatments. Regardless of protocol, reasons for antimicrobial treatment withheld included cow being on a cull list, having a chronic intramammary infection, or being at end of lactation (i.e., close to dry off). If clinical signs persisted after treatment, farmers indicated that they would ask veterinarians for advice, stop treatment, or continue with the same or different antibiotics. Results of this study can be used to design interventions targeting judicious mastitis-related antimicrobial use, and aid discussions between veterinarians and dairy producers regarding CM-related antimicrobial use.

Key words: antimicrobial use, antimicrobial stewardship, decision making, protocol, bovine mastitis

INTRODUCTION

Because antimicrobial use (**AMU**) is correlated with antimicrobial resistance (**AMR**), and strong indications exist that prevalence of AMR in livestock is associated with AMR in humans (Woolhouse et al., 2015), societal pressure has increased to reduce AMU in livestock (McCubbin et al., 2021). The World Health Organization declared that AMR is one of the top 10 global public health threats (eClinicalMedicine, 2021; WHO, 2021). Although contribution of dairy-related AMU to the abundance of AMR genes is less than in other livestock sectors such as swine and poultry (He et al., 2020), AMU on dairy farms puts workers who are in close contact with cattle at risk of attracting AMR genes (Tang et al., 2017). In addition, the strong cor-

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*Corresponding author: barkema@ucalgary.ca

relation between AMU and AMR in livestock (Davies and Davies; 2010) threatens animal welfare (Wall et al., 2016).

The majority of AMU on dairy farms is attributed to prevention and treatment of subclinical and clinical mastitis (**CM**; Pol and Ruegg, 2007; Menéndez González et al., 2010; Kuipers et al., 2016; Warder et al., 2023). Subsequently, reports of AMR in mastitis pathogens include *Escherichia coli* producing extended-spectrum β-lactamase (ESBL), which makes up 0.3% of *E. coli* CM cases in France (Dahmen et al., 2013), 6.7% in Greece (Filioussis et al., 2020), and 23% in China (Yang et al., 2018). In Canada, data from 2007 to 2008 identified multidrug resistance in 15% of *Staphylococcus aureus* isolates, 63% in *E. coli* isolates, and 55% in *Klebsiella* isolates, based on milk samples of both healthy cows and CM cases (Saini et al., 2012a). Data from Europe suggest that for most compounds and pathogens, resistance rates have not changed when comparing data from 2009–2012 to 2002–2006 (de Jong et al., 2018). Exceptions were decreasing *Staph. aureus* resistance to penicillin G and increasing resistance of *Streptococcus uberis* to tetracycline (de Jong et al., 2018).

In recent decades, opportunities emerged that allowed a shift away from “blanket” treating all CM cases with antimicrobials. Mastitis control plans, such as the 5-point and then the 10-point plan promoted in countries with a developed dairy industry (Neave et al., 1969; NMC, 2020), have led to a reduction in infection pressure by contagious mastitis pathogens on dairy farms (Zadoks and Fitzpatrick, 2009). As a result, a relatively higher proportion of CM cases are caused by environmental udder pathogens such as *Strep. uberis* and *E. coli* (Zadoks and Fitzpatrick, 2009). Nonsevere CM cases caused by *E. coli* do not require antimicrobial treatment because their spontaneous cure rate is high (Schmenger and Krömker, 2020) and many approved intramammary antibiotics do not target gram-negative bacteria. In addition, in an increasing number of countries, rapid diagnostic testing has become available at most veterinary practices. Commercial on-farm testing methods have also become more accessible (Malcata et al., 2020). Together, these trends allow for adoption of a selective treatment approach (e.g., using outcomes of rapid diagnostic tests to exclude CM cases from antimicrobial treatment, such as those caused by *E. coli*) (de Jong et al., 2023a).

Selective treatment of CM has already been adopted in many countries (de Jong et al., 2023a). A meta-analysis demonstrated that these selective CM treatment protocols do not affect bacteriological cure, clinical cure, recurrence, and other udder health parameters (de Jong et al., 2023b). However, adoption of a selective CM treatment strategy among Canada dairy farms and specifics of such protocols are unknown.

Additionally, in practice, treatment decisions for CM are not solely based on outcomes of rapid diagnostic tests. Considerations also include, among others, milk yield, changes in rumination, previous CM cases, information from DHI reports, and broader farm goals (Vaarst et al., 2002; Kayitsinga et al., 2017). In addition to reviews recommending CM treatment strategies and decision making (Roberson, 2012; Ruegg, 2018; de Jong et al., 2023a), limited information regarding factors involved in CM decision making is available and unknown in Canada. Hence, the objectives of this study were (1) to characterize adoption of CM treatment practices on Canadian dairy farms, and (2) to identify which factors play a role in decision making regarding cow-level CM treatment decisions.

MATERIALS AND METHODS

This study was reviewed and approved by the University of Calgary Conjoint Faculties Research Ethics Board (study ID number REB19–0353). This report was written according to the STROBE-Vet guidelines (Sargeant et al., 2016).

Data Collection

Data for this study were collected in 2019 and 2020 during annual farm visits of 142 farms participating in the Canadian Dairy Network for Antimicrobial Stewardship and Resistance (**CaDNetASR**). Using surveillance questionnaires, AMU data, and analysis of fecal samples, CaDNetASR aims to annually assess AMU and AMR patterns on Canadian dairy farms located in British Columbia, Alberta, Ontario, Quebec, and Nova Scotia (Fonseca et al., 2022). In short, farms were eligible for enrolment if they had >50 milking cows (except for farms located in Nova Scotia, where the minimum herd size was 40 milking cows), were enrolled in regular milk recording DHI, and raised their replacement heifers on site (Fonseca et al., 2022). With increasing numbers of farms using an automatic milking system (**AMS**) in Canada (Tse et al., 2017) and a relatively high proportion of these farms not being DHI participants (Tse et al., 2018), these herds were not required to have DHI data available to satisfy the calculated sample size (Fonseca et al., 2022). Farms were identified through a convenience selection process as veterinary clinics were used to identify eligible farms in each province.

In 2019 and 2020, 2 additional research questionnaires were administered by regional fieldworkers in either English or French during the described annual

CaDNetASR sampling visits (https://data.mendeley.com/datasets/337mvx7nxn/1, McCubbin et al., 2023). Questions pertained to both dry cow therapy and CM treatment practices, with the results regarding dry cow therapy reported elsewhere (McCubbin et al., 2023). In the section on CM treatment practices, farmers were asked during the first visit to specify if they treated all CM cases with antibiotics, and if not, to provide details regarding SCC and CM case history used for treatment selection. These details included time frame and thresholds considered. In addition, farmers were asked to indicate the relative importance of 9 potential decision factors (severity of clinical signs, SCC, suspected or confirmed bacteria in the quarter, CM case history, milk production, need to fill milk quota, age, genetics, culling, and replacement costs) on a 1 to 5 scale with 1 being very important and 5 being not important. During the second visit, farmers were asked for details about milk culturing, special instances in which cows were not treated with antibiotics, and decisions about further actions when clinical signs persist (https://data.mendeley.com/datasets/337mvx7nxn/1, McCubbin et al., 2023). All questions in both questionnaires were multiple choice with the option "other" if their situation was not listed, which prompted a field to answer an alternative response.

The surveillance questionnaires included questions about milking system, housing system, biosecurity, disease incidence, and treatment choices (https://www.frontiersin.org/articles/10.3389/fvets.2021.799622/full#supplementary-material; Fonseca et al., 2022). More specifically, producers were asked for the number of milking cows, how many cows had CM during the previous 12 mo, what percentage of cows with CM received antibiotics, and their first, second, and third choices of antibiotics to treat CM cases on their farm. When data were missing, producers were contacted by the regional field workers to get the responses. Each farm was visited twice with 10 to 14 mo between visits. The DHI data were retrieved from Lactanet (Guelph, ON, Canada; Sainte-Anne-de-Bellevue, QC, Canada) with producer consent for all cows present on the study farms during 2019.

Data Management

Responses to the research and surveillance questionnaires were entered into Excel (Microsoft Corp., Redmond, WA) spreadsheets. DHI data were made available as text files. Excel and text files were imported into R using RStudio version 1.2.5033 (R Core Team 2019, R Foundation for Statistical Computing, Vienna, Austria). In those instances where surveillance data from 2019 were not available, 2020 data were used (n = 5).

Medians and interquartile ranges (**IQR**) were calculated from the surveillance questionnaire and reported for the self-reported number of milking cows, number of CM cases per 100 cows/year, and percent of CM cases receiving antimicrobial treatment. Proportions were calculated and reported for the use of various milking systems, housing systems, and self-reported antimicrobial treatment preferences for CM. From the research questionnaires, medians and IQR were calculated and reported for SCC thresholds, proportions were calculated and reported for various considerations regarding CM case history, SCC considerations, special exemptions from antimicrobial treatment protocols, and decisions to switch antimicrobial treatments. Geometric mean and standard deviation bulk tank SCC were calculated from DHI data. From cow-level data, SCC were averaged per cow over all DHI visits in 1 calendar year (excluding DHI test dates within the dry period) and used to calculate and report geometric means at the herd level.

Statistical Analyses

Logistic regression was used to analyze the association of the self-reported use of a selective CM treatment protocol in 2019 with herd characteristics (no. of lactating cows, no. of CM cases per 100 cows/year, average cow SCC, bulk tank SCC, province, milking system, and housing system). Continuous independent variables were checked for linearity in the logit scale and categorized when needed. Collinearity was assessed with Pearson correlation for continuous variables, and Cramer's V for nominal variables. Univariable associations were identified between the herd characteristics and self-reported use of selective CM treatment protocol; variables with $P < 0.25$ were selected for multivariable modeling. Covariates that confounded the association between each herd characteristic and reported use of selective CM treatment protocols were identified using a directed acyclic graph (Supplemental Figure S1; https://data.mendeley.com/datasets/h48vb4dds6/1; de Jong, 2023). Subsequently, for each herd characteristic, a multivariable logistic model was made with the outcome that included relevant covariates to obtain accurate effect estimates. Odds ratios of the variables, their 95% confidence intervals, and *P*-values were reported.

To identify subsets of farms present in the data with similar decision "profiles," a multivariate analysis (cluster analysis) was conducted. Variables included were 9 decision factors (production of the cow, severity of clinical signs, high SCC, CM case history, suspected or confirmed bacteria, need to fill milk quota, cull and replacement costs, cow age, cow genetics) to which

Table 1. Milking and housing systems [% (n)] among 142 Canadian farms across 5 provinces surveyed in 2019 and 2020

	Milking system				Housing system			
Province	Parlor	AMS[1]	Pipeline	>1 system	Freestall	Tiestall	Pack stall	>1 system
British Columbia	57 (17)	37 (11)	3 (1)	3 (1)	93 (28)	0 (0)	0 (0)	7 (2)
Alberta	77 (23)	23 (7)	0 (0)	0 (0)	90 (27)	0 (0)	3 (1)	7 (2)
Ontario	48 (15)	42 (13)	10 (3)	0 (0)	87 (27)	10 (3)	3 (1)	0 (0)
Quebec	22 (6)	11 (3)	67 (18)	0 (0)	11 (3)	52 (14)	0 (0)	37 (10)
Nova Scotia	38 (9)	17 (4)	42 (10)	4 (1)	54 (13)	38 (9)	0 (0)	8 (2)
All provinces	49 (70)	27 (38)	23 (32)	1 (2)	70 (98)	18 (26)	1 (2)	11 (16)

[1]Automated milking system.

producers indicated importance on a 5-point scale from "very important" to "not important." A multiple latent block model based on a stochastic binary search algorithm was used (Biernacki and Jacques, 2016). This specific model was chosen over alternatives (such as k-means clustering, partitioning around medoids, and principal component analysis) because of the ordinal nature of the data. Number of clusters was determined using the gap statistic from the R package 'cluster' (Tibshirani et al., 2001; Maechler et al., 2022). Subsequently, clusters were identified using 'bosclust' from R package 'ordinalClust' (Selosse et al., 2020) and visualized using the R packages 'sjPlot' (Daniel Lüdecke, 2023) and 'ggplot2' (Wickham, 2016).

RESULTS

In total, 142 farms completed the surveillance and research questionnaires (British Columbia = 30; Alberta = 30; Ontario = 31; Quebec = 27; and Nova Scotia = 24). Of these farms, 70% housed their milking herd in a freestall, 18% in a tiestall, 2 farmers had a straw pack stall, and 11% had a combination of different housing systems (Table 1). Regarding milking system, 49% milked in a parlor, 27% milked with an AMS, 23% used a pipeline system, and 1% had a combination of milking systems (Table 1).

Median herd size was 108 lactating cows (IQR 109 cows), which varied between provinces from 73 lactating cows in Nova Scotia to 161 lactating cows in British Columbia (Table 2). Of the farms with DHI data available, median cow 305-d milk yield per herd was 10,706 kg (IQR 1,704 kg; n = 130 farms) and geometric mean cow SCC per herd was 53,271 cells/mL (SD 21,605 cells/mL; n = 128 farms). Bulk tank SCC was available for 118 herds, as not all herds had opted into SCC testing, and geometric mean bulk tank SCC was 203,055 cells/mL (SD 80,663 cells/mL; Table 2). Of the farms that were not enrolled in DHI milk recording at time of the questionnaire, 6 milked with AMS and 6 were milking in a parlor. Self-reported median incidence of CM over the previous 12 mo at time of the questionnaires was 16 cases per 100 cow/year (IQR 17 cases per 100 cow/year; Table 2).

Treatment of Clinical Mastitis

Most frequently reported antimicrobials for treatment of CM (Table 3) on farms located in British Columbia, Alberta, Ontario, and Nova Scotia were a product containing a combination of penicillin G procaine, dihydrostreptomycin sulfate, novobiocin sodium, polymyxin B sulfate, hydrocortisone acetate, and hydrocortisone sodium succinate (Special Formula 17900-Forte; Zoetis, Kirkland, QC, Canada), and an intramammary ceftiofur hydrochloride (Spectramast LC; Zoetis). Both products were most frequently reported when considering first choice (35% and 32% of farms, respectively) and among the top 3 antimicrobial treatments per farm (mentioned by 59% and 56% of farms, respectively). Only 136/142 farms answered this section of the questionnaire.

In one province, Quebec, a regulation against usage of category I antimicrobials (e.g., ceftiofur, polymyxin B sulfate) as a first line of treatment was adopted early in 2019 (Roy et al., 2020). As such, the most frequently reported antimicrobial for treatment of CM in Quebec was intramammary pirlimycin (Pirsue; Zoetis, Kirkland, QC, Canada; Table 3), both when considering first choice (52% of farms) and among the top 3 antimicrobial treatments per farm (63% of farms).

Self-reported adoption of selective CM treatment protocols was 64% (Table 4); these farms treated a median proportion of 82% cows with CM in 2019. Association between selective treatment of CM and herd size, CM incidence, mean herd average cow SCC, province, milking system, and housing system was assessed using univariable (Table 5) and multivariable (Table 6) logistic regression modeling. As housing system and milking system were correlated, only milking system was further explored in relation to adoption of selective CM protocols because it had a lower univariable P-value. Similarly, as herd average cow SCC and bulk tank SCC were correlated, only herd average cow SCC was further explored in relation to adoption of selective CM pro-

Table 2. Herd size, production parameters, and clinical mastitis (CM) incidence among 142 Canadian farms across 5 provinces in 2019

	No. of lactating cows[1]			Avg cow 305-d milk yield[2] (kg)			Avg cow SCC[2] (× 1,000 cells/mL)			Avg bulk tank SCC[2] (× 1,000 cells/mL)			No. of CM cases[1] (per 100 cows/yr)		
Province	n	Median	IQR	n	Median	IQR	n	Mean[3]	SD	n	Mean[3]	SD	n	Median	IQR
British Columbia	30	161	154	25	11,007	2,011	25	43.1	18.8	22	190	76	29	15	13
Alberta	30	152	94	29	10,827	1,489	28	59.2	27.2	24	239	99	30	22	17
Ontario	31	108	126	27	10,928	1,373	26	51.9	13.4	24	190	54	31	12	19
Quebec	27	75	47	26	10,516	964	26	50.6	19.0	25	189	78	27	18	15
Nova Scotia	24	73	70	23	10,179	2,039	23	61.7	23.3	23	209	83	24	15	16
All provinces	142	108	109	130	10,706	1,704	128	53.3	21.6	118	203	81	141	16	17

[1]Self-reported. Five farms did not have 2019 survey data available; 2020 survey data were used instead. IQR = interquartile range.

[2]DHI records. Means and medians were calculated per cow across all available reports in 2019, then averaged (Avg) per farm.

[3]Geometric mean.

Table 3. Antimicrobial preferences [% (n)] to treat clinical mastitis[1]

			British Columbia, Alberta, Ontario, Nova Scotia		Quebec	
Active ingredient	Administration route[2]	Brand name	First choice	Top 3	First choice	Top 3
Penicillin G procaine, dihydrostreptomycin, novobiocin, polymyxin B	IMM	Special Formula 17900-Forte	35 (38)	59 (64)	7 (2)	33 (9)
Ceftiofur	IMM	Spectramast LC	32 (35)	56 (61)	11 (3)	41 (11)
Cephapirin	IMM	Cefa-Lak	18 (20)	35 (38)	22 (6)	37 (10)
Trimethoprim, sulfadoxine	i.m.	Trimidox, Borgal, Trivetrin, Norovet	7 (8)	33 (36)	7 (2)	48 (13)
Pirlimycin	IMM	Pirsue	3 (3)	14 (15)	52 (14)	63 (17)
Ceftiofur	i.m.	Excenel RTU, Excenel suspension	2 (2)	2 (2)	0 (0)	0 (0)
Oxytetracycline	i.m.	Oxyvet 100 LP	1 (1)	2 (2)	0 (0)	15 (4)
Benzylpenicillin procaine/benzathine	i.m.	Depocillin, duplocillin LA	2 (2)	5 (5)	0 (0)	7 (2)
Oxytetracycline	s.c.	Oxymycine 300 LA	0 (0)	1 (1)	0 (0)	4 (1)
Ceftiofur	s.c.	Excede	0 (0)	1 (1)	0 (0)	0 (0)

[1]Survey was distributed among 142 Canadian dairy farmers across 5 provinces; complete data were available for 136 farms. Farms were asked to indicate their first, second, and third choices of antibiotics to treat clinical mastitis cases. Quebec is displayed separately due to regulations implemented in 2019.

[2]IMM = intramammary.

Table 4. Percentage of farms that used a selective clinical mastitis (CM) treatment protocol (self-reported) among 142 Canadian farms across 5 provinces in 2019, and percentage of cows with CM treated in the previous 12 mo with antimicrobials on all farms (n = 142), farms with selective (n = 91), and blanket CM treatment protocols (n = 51)

		Percentage CM treated[1]					
		All		Selective		Blanket	
Province	Selective % (n)	Median	IQR	Median	IQR	Median	IQR
British Columbia	67 (20)	85	48	60	45	100	10
Alberta	47 (14)	100	18	75	45	100	0
Ontario	61 (19)	100	0	100	0	100	0
Quebec	78 (21)	79	50	60	40	100	0
Nova Scotia	71 (17)	90	50	90	30	100	50
All provinces	64 (91)	100	40	82	50	100	0

[1]Five farms did not have 2019 survey data available; 2020 survey data were used instead. IQR = interquartile range.

tocols because there were fewer missing observations. Complete data, including DHI data, were available from 128/142 farms. The odds to implement a selective CM treatment protocol increased with a decreasing average cow SCC ($P = 0.046$), which is visualized in Figure 1. Although in the univariable analysis, farms with selective CM treatment protocols had a smaller herd size than farms with blanket CM treatment protocols ($P = 0.03$), herd size was not significantly associated with selective treatment of CM ($P = 0.15$) when evaluated in multivariable logistic regression.

Treatment Decision Factors

Three clusters of farms were differentiated based on importance assigned to the 9 decision factors for cow-level CM treatment decisions: those basing their decision on "severity" (n = 12 farms) versus "udder health" (n = 12 farms) versus "cow health" (n = 66 farms; Figure 2; Supplemental Table S1, https://data.mendeley.com/datasets/h48vb4dds6/1; de Jong, 2023). Data were unavailable for 1 farm that used a selective CM treatment protocol.

Table 5. Association between adoption of selective treatment of clinical mastitis (CM) and herd characteristics using a univariable logistic regression model[1]

	% (n) or median [IQR]		
Variable	Selective	Blanket	Univariable *P*-value
Herd size (lactating cows)	93 [79]	144 [124]	0.03
No. of CM cases per 100 cows/year	16 [17]	18 [18]	0.44
Avg[2] cow SCC (× 1,000 cells/mL)	48 [22]	56 [19]	0.06
Avg[2] bulk tank SCC[3] (× 1,000 cells/mL)	177 [73]	216 [12]	0.10
Province			0.14
British Columbia	60 (15)	40 (10)	0.32
Alberta	46 (13)	54 (15)	Referent
Ontario	62 (16)	38 (10)	0.27
Quebec	77 (20)	23 (6)	0.02
Nova Scotia	74 (17)	26 (6)	0.05
Milking system			0.09
Parlor	61 (39)	39 (25)	Referent
Pipeline	78 (25)	22 (7)	0.10
AMS[4] and >1 milking system	53 (17)	47 (15)	0.46
Housing system			0.38
Tiestall	73 (19)	27 (7)	Referent
Freestall	59 (51)	41 (35)	0.21
Straw pack and >1 housing system	69 (11)	31 (5)	0.76

[1]Survey was distributed among 142 Canadian dairy farmers across 5 provinces; complete data were available for 128 farms, of which 81 indicated that they treated mastitis selectively, whereas 47 used blanket treatment. IQR = interquartile range.

[2]Geometric mean. Avg = average.

[3]Missing data from 10 herds.

[4]Automated milking system.

Table 6. Association between adoption of selective treatment of clinical mastitis (CM) and herd characteristics using multivariable logistic regression models[1]

Variable	β	Odds ratio	95% CI	*P*-value	Covariates[2]
Herd size (lactating cows)	−0.003	1.00	0.99–1.00	0.17	Province, milking system
Avg[3] cow SCC (× 1,000 cells/mL)	−0.02	0.98	0.69–1.15	0.04	CM incidence, herd size
Province				0.52	Herd size, milking system
British Columbia	Referent				
Alberta	−0.70	0.50	0.15–1.53	0.23	
Ontario	−0.06	0.94	0.29–3.01	0.92	
Quebec	0.33	1.39	0.33–6.14	0.65	
Nova Scotia	0.32	1.38	0.37–5.36	0.64	
Milking system				0.44	Herd size, province
Parlor	Referent				
Pipeline	0.02	1.02	0.28–3.77	0.98	
AMS[4] and >1 milking system	−0.56	0.57	0.22–1.42	0.23	

[1]Survey was distributed among 142 Canadian dairy farmers across 5 provinces; complete data were available for 128 farms.

[2]Covariates included as confounders to adjust the estimate of the variable.

[3]Geometric mean. Avg = average.

[4]Automated milking system.

The "severity" cluster consisted of farms where decisions were based almost exclusively on severity of signs. The decision factor "severity of symptoms" was "very important" for 83% of farms in this cluster, whereas hardly any other factors were considered important. The "udder health" cluster consisted of farms in which, in addition to severity, other udder health indicators were also taken into consideration. As such, suspected or confirmed bacteria was listed as "very important" or "important" by 75% of the farms in this cluster and CM case history by 64%. The "cow health" cluster consisted of farms that, in addition to udder health indicators, also incorporated information regarding the cow. As such, SCC was listed as "very important" or "important" by 65% of the farms in this cluster, and production of the cow by 58%. In all 3 clusters, need to fill milk quota, cull and replacement costs, age, and genetics were relatively infrequently listed as "very important" or "important."

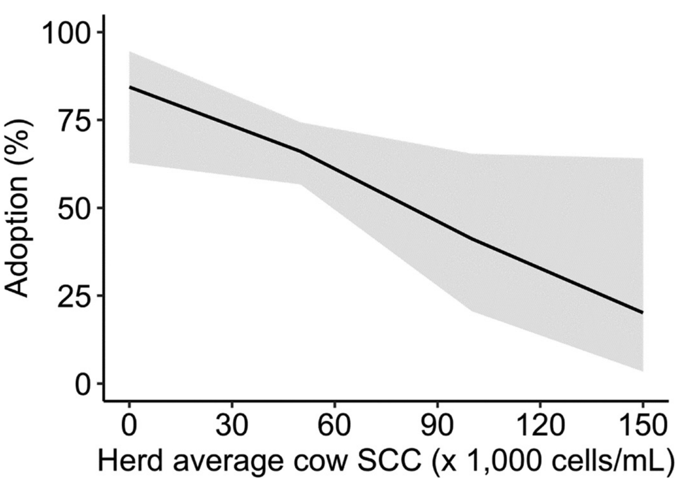

Figure 1. Association between herd average lactating cow SCC and predicted adoption of selective clinical mastitis treatment protocols. Predictions were made using a multivariable logistic regression model presented in Table 6, using available data of 128 Canadian farms across 5 provinces in 2019.

Of the farms that considered CM case history among their decision factors (n = 58 farms), 71% answered detailed questions due to design of the questionnaire (Table 7). Most farmers (66%) only considered number of previous CM cases, ranging from >1 CM in current lactation or >2 CM in past month, to >3 CM in previous lactation. Other (14%) farmers considered only the time point of the previous CM case (e.g., whether a potential previous CM case occurred in the current lactation or previous month). Some (10%) farmers considered a combination of number of CM and time point of previous CM.

Of the farms that considered SCC among their decision factors (n = 47 farms), 74% answered detailed questions (Table 7). Somatic cell count thresholds were considered by the majority of farmers (83%) and median cow SCC threshold considered was 300,000 cells/mL (range 150,000–1,000,000; IQR 275,000 cells/mL). Most farmers (62%) used last DHI record available, followed by last 3 records. Some farmers (14%) did not use a specific threshold and judged on per-cow bases, and others (9%) indicated using the AMS attention list.

Of the farms that considered suspected or confirmed bacteria identified in the CM sample among their decision factors (n = 57 farms), 82% answered detailed questions (Table 7). Farms indicated that they made use of diagnostic services from their veterinary clinic (74%), provincial laboratories (21%), and on-farm culture systems (13%). Two (4%) farms indicated that they made use of DHI laboratory. All farms indicated

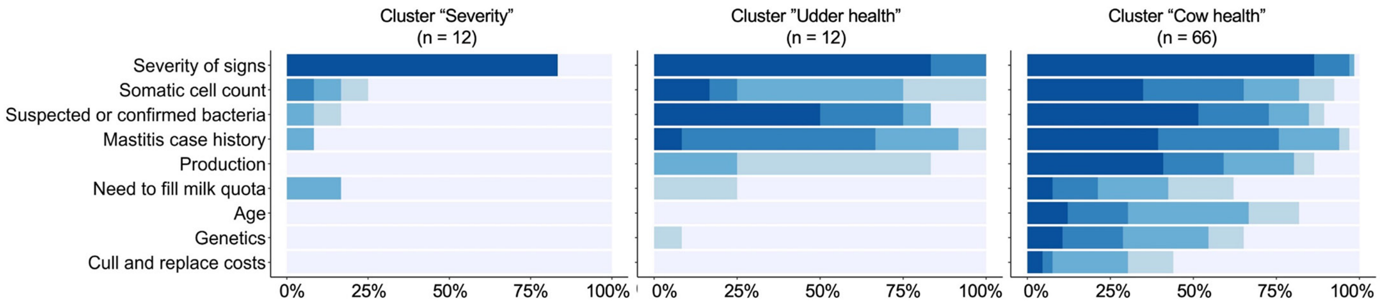

Figure 2. Visualization of 3 profiles of farmers based on the importance assigned to 9 decision factors for antimicrobial treatment of clinical mastitis (CM). For each decision factor, the proportion (%) is displayed of farms that indicated importance on a 5-point scale, ranging from very important (dark blue) to not important (gray). Survey was distributed among 142 Canadian dairy farmers across 5 provinces, of which 91 farmers indicated that they selectively treated CM. Data regarding decision factors were available for 90 farms.

Table 7. Responses to follow-up questions regarding treatment decisions for clinical mastitis (CM)[1]

Decision factor	Additional information	% of farms (n)
CM case history (n = 41)	Considers only time point of the previous CM	24 (10)
	Current lactation	40 (4)
	Past month	30 (3)
	Past 3 mo	20 (2)
	Current and previous lactation	10 (1)
	Considers only number of CM cases	66 (27)
	>1 CM in current lactation	30 (8)
	>2 CM in current lactation	22 (6)
	>3 CM in current lactation	11 (3)
	Unspecified number of CM in current lactation	11 (3)
	>2 CM in past month	11 (3)
	>3 CM in past month	4 (1)
	>1 CM in previous lactation	4 (1)
	>2 CM in previous lactation	4 (1)
	>2 CM in current, >3 in previous lactation	4 (1)
	Considers both previous CM and number of CM cases	10 (4)
	CM in past month, >1 CM in current lactation	25 (1)
	CM in current lactation, >1 CM in previous lactation	50 (2)
	CM in current lactation, >2 CM in previous lactation	25 (1)
SCC (n = 35)	SCC threshold (median 300,000 cells/mL, IQR 275,000)	83 (29)
	Last SCC record	62 (18)
	Last 2 SCC records	3 (1)
	Last 3 SCC records	21 (6)
	Current lactation	7 (2)
	Automated milking system attention list	9 (3)
	Judgment per cow	14 (5)
Suspected or confirmed bacteria (n = 47)	Diagnostic services[2]	
	Veterinary clinic	74 (35)
	Provincial laboratory	21 (10)
	On-farm system	13 (6)
	DHI laboratory	4 (2)
	Level of results[2]	
	Bacteria specification	100 (47)
	Sensitivity to antibiotics	30 (14)
	Use of culture results[2]	
	Start treatment	53 (25)
	Change treatment	60 (28)
	Stop treatment	23 (11)
	Does not use results to start, change, or stop	11 (5)
	Inform herd status	4 (2)
	Consult veterinarian	2 (1)
	Culling decisions	2 (1)

[1]Survey was distributed among 142 Canadian dairy farmers across 5 provinces, of which 91 farmers indicated that they selectively treated CM. Among the decision factors used, 58 farmers used CM case history, of which 41 answered follow-up questions; 47 farmers used SCC, of which 35 answered follow-up questions; 57 farmers used suspected or confirmed bacteria, of which 47 answered follow-up questions. IQR = interquartile range.

[2]Multiple answers possible.

Table 8. Responses to questions regarding antimicrobial treatment decisions for clinical mastitis[1]

Item	Reason	% of farms (n)
Reasons to withhold antimicrobial treatments	On cull list	65 (59)
	Chronic infection	47 (43)
	End of lactation	31 (28)
	High yielding cow	18 (16)
	First half of lactation	13 (12)
	Behavior not affected	3 (3)
Actions when clinical signs persist after treatment	Ask veterinarian for advice	40 (36)
	Continue with different antibiotic	35 (32)
	Stop treatment	32 (29)
	Continue with same antibiotic	25 (23)
	Culture milk sample	19 (17)
	Put cow on cull list	16 (15)
	Dry off quarter	10 (9)
	Dry off early	4 (4)
	Euthanasia	2 (2)

[1]These questions were presented to 91 farmers across Canada who indicated that they selectively treated CM (multiple answers possible).

that test results provided bacteria identification at either the genus or species level (such as *Staph. aureus*, streptococci); some farms (30%) also received sensitivity against different antimicrobials. Most farms used the culture results to decide which treatment to start, to change the initial treatment, or stop the treatment. Other infrequent uses for test results were to inform herd status, to consult the herd veterinarian, and to make culling decisions.

Additionally, farmers indicated that they may withhold antimicrobial treatment if the cow is on the cull list, if the cow has a chronic IMI, if the CM case occurs at the end of the cow's lactation, if the cow is a high yielding cow, and if the CM case occurs in the first half of lactation (Table 8). Some (3%) farmers indicated that they would not treat if the behavior of the cow did not seem to be affected (including rumination).

When clinical signs persisted at the end of the chosen treatment, farmers indicated that they may (Table 8) continue treatment with the same antibiotic, continue treatment with a different antibiotic, stop treatment, ask veterinarian for advice, culture milk sample, put the cow on cull list, or dry the quarter off. Some (4%) farmers indicated that they would dry off early, or suggested euthanasia when signs persist (2%).

DISCUSSION

This study provided an estimate of the proportion of farms in Canada adopting a selective CM treatment approach and characterized 3 profiles of selective CM treatment farms based on cow-level decision factors (i.e., treatment based on severity, udder health, and cow health parameters).

A high uptake (64%) was reported of self-reported selective CM treatment protocols. In contrast, a study among eastern US farmers reported 45% of farms used selection criteria for treatment of CM (Kayitsinga et al., 2017). Regardless of the high uptake of these selective protocols, reported proportion of cases receiving antimicrobial treatment among those farms using selective treatment protocols was high (82% [IQR 40%]). This can partly be attributed to farmers who indicated using a selective CM protocol, but also indicated treating all CM cases in 2019. This is possible when all cases occurring in a certain calendar year fall outside the selection criteria for not using antimicrobials, especially if the criteria are quite limiting and only include severity. Farmers might also have been inclined to provide a more desirable answer than the on-farm treatment situation; this does, however, not explain the occurrence of farms treating <100% while self-identifying as blanket CM protocol farms. Regardless, reported proportion of cases receiving antimicrobial treatment in the total study population (both selective and blanket farms) was higher than a study with a similar Canadian study population (100% [IQR 40%] vs. 90%; Aghamohammadi et al., 2018).

Lower herd average of milking cow SCC on DHI tests, likely the result of a higher proportion of low SCC cows, was associated with increased likelihood of having a selective CM treatment protocol. A low average cow SCC is indicative of good herd udder health (Schukken et al., 2003), with high average cow SCC or bulk milk SCC associated with a relatively high incidence of CM caused by contagious pathogens such as *Staph. aureus* and a lower incidence of CM caused by *E. coli* (Barkema et al., 1998; Olde Riekerink et al., 2008). This suggests that farms with better udder health are inclined to use selective treatment approaches. Absence of other associations between uptake of a selective CM treatment protocol and farm characteristics such as province, milking system, and incidence of CM cases, raises questions about potential unexplored factors that may influence decision making. Research on antimicrobial decision making suggests that personal beliefs, values, and perceptions also play a role (Kayitsinga et al., 2017; Rees et al., 2021), which therefore could have contributed to the variation in adoption of selective CM treatment protocols.

The 3 identified decision-making profiles accentuate different attitudes toward CM protocols, ranging from protocols that only include 1 factor ("severity"), to protocols where many different factors are considered ("cow health"). Although, reported importance of severity, high SCC and suspected pathogen are in agreement with research from Denmark and the eastern United States (Vaarst et al., 2002; Kayitsinga et al., 2017; Wilm et al., 2021), the identification of different profiles deviates from existing knowledge on mastitis decision making based on interviews with Danish dairy farmers in the early 2000s (Vaarst et al., 2002). Vaarst et al. (2002) described how decisions are being made on 4 levels: severity of signs, cow characteristics (e.g., SCC, CM case history, lactation stage, reproduction status, and value of the cow), herd goals (e.g., availability of replacement heifers, bulk tank SCC, milking preferences), and alternatives (e.g., drying of a quarter, drying the cow off early). Awareness of differences in on-farm mastitis decision making facilitates a tailored approach to antimicrobial stewardship initiatives.

The profiles also highlight varied definitions of selective CM protocols between farmers and the scientific community. The majority of the surveyed farmers belonging to the "severity" profile only used severity of clinical signs to make treatment decisions. In contrast, in the scientific community, use of rapid diagnostic tests is a key characteristic of a selective CM protocol (de Jong et al., 2023a). This discrepancy demands an agreement on terminology to monitor uptake of interventions aimed to improve antimicrobial stewardship such as selective CM treatment protocols.

Most frequently used antimicrobials to treat CM were intramammary ceftiofur hydrochloride and an intramammary combination of penicillin G procaine, dihydrostreptomycin sulfate, novobiocin sodium, and polymyxin B, followed by intramammary cephapirin. These findings are in line with other studies in Canada and the United States (Pol and Ruegg, 2007; Saini et al., 2012b), which suggests that antimicrobial drug choices have remained stable in the last decades. According to the WHO, cephapirin has been listed as a highly important antimicrobial, while ceftiofur, dihydrostreptomycin, and polymyxin B are listed as critically important antimicrobials for human health (WHO, 2018). These antimicrobials are often the only available therapies available to treat life-threatening infections in humans or are used to treat infections of bacteria or bacteria carrying AMR genes acquired through nonhuman pathways (WHO, 2018). As such, the patent for Special Formula 17900-Forte was not renewed and is no longer available in Canada for treatment of CM (Health Canada, 2021). Another frequently used drug, Pirsue (pirlimycin hydrochloride), is also no longer available (Health Canada, 2022). This will likely cause a shift in antimicrobial drug preferences similar to the ones observed in Europe (Preine et al., 2022).

Proportion of selective CM farms that use SCC as a criterion (52%) is in line with a survey among eastern US producers (Kayitsinga et al., 2017). Most farms indicated using cow SCC as a selection criterion for CM treatment selection and based their decisions on DHI reports. Use of SCC data is encouraged in selective CM treatment protocols, predominantly to identify cases that have chronic IMI (de Jong et al., 2023a). A threshold of SCC >200,000 cells/mL is typically advised (Gonçalves et al., 2020), based on the previous 2 to 3 DHI reports. However, as the farms in the study sample indicated using predominantly the last DHI record available (instead of the last 2–3 reports) and upholding a threshold of 300,000 cells/mL (higher than the threshold for CM), SCC data were most likely used to assess current udder health status instead of estimating presence of chronic IMI.

To identify bacterial agents in CM cases, both veterinary and provincial laboratories were favored over the use of on-farm testing options. As the farms in the sample averaged 1 to 2 CM cases per month, slower return on investments in training and equipment, and reduced opportunity for trained staff to keep skills up to date, might have contributed to the lower adoption of on-farm rapid test options (Lago and Godden, 2018). Additionally, these relatively smaller farms with only a few cases per month will have an insufficient use of ingredients for on-farm testing, resulting in ingredients not being used before the expiry date. Only a few farms tested for pathogens through DHI (Lactanet), which uses a commercial PCR to determine the presence of only 4 selected pathogens, *Staph. aureus*, *Streptococcus agalactiae*, *Mycoplasma bovis*, and *Prototheca* spp. (Lactanet, 2023). Proportion of farmers making use of diagnostic test options (52%) is lower than reports from Germany (Falkenberg et al., 2019) and from eastern US farmers (Kayitsinga et al., 2017). All farms using bacteriological testing received results on species level, with some also receiving antimicrobial sensitivity. This level of detail allows for a more tailored protocol than those recommending treatment based on cell wall characteristics (gram-positive vs. gram-negative; de Jong et al., 2023a).

Extended antimicrobial treatment when clinical signs persisted was considered by 25% of surveyed farmers, similar to findings by Aghamohammadi et al. (2018). Presence of flakes and swelling of the quarter were also mentioned among German farmers as reasons to extend antimicrobial therapy (Falkenberg et al., 2019). Although extended use of certain antimicrobial treatments will result in more favorable outcomes (Krömker et al., 2010; Swinkels et al., 2013; Truchetti et al., 2014), clinical signs are not a good indicator for projected bacteriological cure (Pinzón-Sánchez and Ruegg, 2011). Therefore, veterinary consultation and bacteriological testing are recommended before extending a treatment.

The present study has several limitations, including sampling bias as farms were not randomly selected, but instead chosen through a network of veterinarians at each site (Fonseca et al., 2022). Although each sampling site was chosen carefully, and farms were enrolled to mirror farm demographics of each province, caution should be exercised when extrapolating presented data to the broader Canadian dairy population. The design of the survey also introduced information bias as farmers were asked to recall disease burden of a variety of diseases and disorders over the previous 12 mo, this time frame could have limited the ability to recall self-reported CM incidence and proportion of cows with CM that received antimicrobial treatment. As a result, the reported CM incidence might underestimate true CM incidence in the study population. In addition, uptake of selective CM protocols has likely been confounded by the presence of progressive dairy farms in our sample. Study participation was voluntary and co-participation in CaDNetASR was required. We were also unable to identify all considerations for antimicrobial CM treatment decisions. In contrast to Vaarst et al. (2002), cow age, cow genetics, culling and replacement costs, and need for milk to fill milk quota were not deemed important by many of the farmers in our study. Conducting personal interviews as an alternative to questionnaires would be capable of alluding to a wider range of treatment considerations and perspectives on antimicrobial stewardship. Furthermore, questionnaire length and duration restrictions limited our ability to include questions regarding dosage and duration of treatments, alternatives to antimicrobial treatments, and chronic CM cases (including definitions, treatment decisions, and consulted information sources).

Results of this study can be used to aid discussions between veterinarians and dairy producers regarding CM-related AMU. More specifically, the different decision-making profiles demonstrate that even among those farms that have implemented selective treatment strategies, uptake of rapid diagnostic testing can be improved, as well as the use of SCC reports to make decisions on a per-case basis. In combination with clear communication regarding bacteriological cure, inclusion of rapid diagnostic tests in selective treatment protocols can further reduce mastitis-related AMU (de Jong et al., 2023a).

CONCLUSIONS

Among 142 farms across 5 provinces in Canada, self-reported uptake of selective CM protocols was 64% and further evaluation of protocols revealed 3 types of protocols: selection based on severity only, selection including udder health parameters, and selection including cow factors as well. Farms with a lower average cow SCC more often implemented a selective CM treatment protocol. These results can be used to aid discussions between veterinarians and dairy producers regarding CM-related AMU.

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ORCIDS

Ellen de Jong https://orcid.org/0000-0002-4198-7898
Kayley D. McCubbin https://orcid.org/0000-0003-4654-2705
Tamaki Uyama https://orcid.org/0000-0002-2252-3043
David F. Kelton https://orcid.org/0000-0001-9606-7602
Simon Dufour https://orcid.org/0000-0001-6418-0424
Luke C. Heider https://orcid.org/0000-0003-3780-7011
Herman W. Barkema https://orcid.org/0000-0002-9678-8378