J. Dairy Sci. 105:6251–6260
https://doi.org/10.3168/jds.2021-21504

Associations of somatic cell count with milk yield and reproductive performance in grazing dairy cows

R. Rearte,[1,2] S. G. Corva,[1] R. L. de la Sota,[1,2] I. M. Lacau-Mengido,[1,3] and M. J. Giuliodori[1]*
[1]Instituto de Investigaciones en Reproducción Animal (INIRA), Facultad de Ciencias Veterinarias-Universidad Nacional de La Plata (FCV-UNLP), La Plata, B1900AVW, Argentina
[2]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, C1033AAJ, Argentina
[3]Instituto de Biología y Medicina Experimental (IByME)-CONICET, Buenos Aires, C1428ADN, Argentina

ABSTRACT

Poor udder health status can have a detrimental effect on milk yield and reproductive performance, leading to reductions in the dairy farm profit. The objective of this retrospective longitudinal study was to assess the associations of somatic cell count (SCC) with daily milk yield and reproductive performance. A database with 1,930,376 lactations from 867 Argentinean grazing dairy herds records collected for 14 years was used. The association of the evolution of SCC (healthy vs. new case vs. cured vs. chronic; with 150,000 SCC/mL as threshold) and of the severity of SCC [mild (150,000–400,000 SCC/mL) vs. moderate (400,000–1,000,000 SCC/mL) vs. severe (>1,000,000 SCC/mL)] with the odds for conception were estimated. Finally, the associations of the linear score of SCC (LS-SCC) with daily milk yield were estimated depending on parity and milk production quartile. The odds ratios (CI 95%) for conception at first service were 0.921 (0.902–0.941), 0.866 (0.848–0.884), and 0.842 (0.826–0.859) for the new case, cured, and chronic cows compared with healthy cows, respectively. Also, the odds ratios (CI 95%) for conception were 0.902 (0.881–0.925), 0.837 (0.808–0.866) and 0.709 (0.683–0.736) for mild, moderate and severe cases compared with healthy cows, respectively. An increase of one point of LS-SCC was associated with decreases of 0.349, 0.539, and 0.676 kg in daily milk yield for first-, second-, and third-lactation cows, respectively. In conclusion, SCC is negatively associated with the risk for conception and with daily milk yield in grazing dairy cows. This negative relationship with conception is higher when SCC increase occurs after the service date and it is influenced by severity of mastitis, and in the case of milk yield, the negative association is influenced by parity, milk production quartile, and severity of mastitis.

Key words: somatic cell count, milk production, reproductive efficiency, grazing dairy cow

INTRODUCTION

Milk yield and reproductive performance are the main determinants of dairy enterprise profit, and udder health status is a factor that has a detrimental effect on both traits (Giordano et al., 2012; Krpalkova et al., 2016). Fitting models to assess the effect of mastitis on the performance of dairy herds is critical to get reliable estimations of economic impact of intervention to control udder diseases (Hagnestam-Nielsen and Østergaard, 2009; Hudson et al., 2015; Vissio et al., 2015).

When an intramammary infection occurs, a flow of inflammatory cells is the normal defensive response. The increase of SCC in milk is a good indicator of intramammary infection (Ruegg and Erskine, 2014). Previous studies have estimated the effect of SCC on different indicators of reproductive performance, such as longer days to first service (Barker et al., 1998; Schrick et al., 2001; Pinedo et al., 2009), lower conception risk (Lavon et al., 2011a; Hudson et al., 2012; Hertl et al., 2014; Fuenzalida et al., 2015), and higher risk of pregnancy loss (Chebel et al., 2004; Pinedo et al., 2009). Even if the size of the association estimated among those studies are not directly comparable due to differences in study designs and indicators of udder health status used (clinical mastitis records, periodic SCC records, or a combination of both), the most deleterious effect occurred when mastitis events took place after insemination, and when the severity of the cases increased (Lavon et al., 2011a; Hudson et al., 2012; Hertl et al., 2014; Fuenzalida et al., 2015). These field observations agree with other experimental studies showing that mastitis events could alter the hormonal profile leading to pregnancy failure (Herath et al., 2007; Lavon et al., 2011b). Mastitis events can have a carryover effect of almost 60 d when occurring before

Received October 29, 2021.
Accepted March 14, 2022.
*Corresponding author: mauriciog1969@gmail.com

artificial insemination (Hudson et al., 2012), supporting the hypothesis that the inflammatory process in the udder could damage the preovulatory oocytes (Roth et al., 2013; Furman et al., 2014). Also, the effect of mastitis in early lactation has been shown to disrupt early embryo development during the preimplantation period with reduced morula quality, conceptus elongation, and embryo survival in dairy cows (Ribeiro et al., 2016). In addition, the detrimental effect of mastitis events on conception rate, occurring between service date and pregnancy diagnosis, could be explained by the inflammatory response causing luteolysis due to $PGF_{2\alpha}$ release, leading to early embryonic loss (Santos et al., 2004).

Several studies performed across the world have addressed the effect of mastitis on milk yield loss. Among those studies, different mastitis indicators and statistical approaches have been used to model the mean effect of mastitis on milk yield, reporting a wide range of results. Thus, a cow with 200,000 SCC/mL will lose (compared with the baseline of 50,000 SCC/mL) between 0.28 and 0.8 kg/d in first-parity cows, between 0.61 and 1.43 kg/d in second-parity cows, and between 0.63 and 2.41 kg/d in third-parity cows (Hortet et al., 1999; Dürr et al., 2008; Halasa et al., 2009; Hand et al., 2012; Boland et al., 2013). In those studies, the linear transformation of SCC allowed to describe the relationship between milk production and transformed SCC with linear regression models. The difference could explain variability in these reported results in the population under study, and other risk factors, such as breed, DIM, parity number, and quartile of milk production, all having the potential to modulate the association of SCC with milk yield and reproductive performance have been controlled in different ways or directly ignored in these previous works.

Although several studies have previously addressed the effects of high SCC on milk yield and reproductive performance, most of those studies have not fully addressed how the relationship estimated between such traits at the cow level could be influenced by characteristics at the herd level. To the best of our knowledge, there is a need for studies assessing the association of SCC with productive and reproductive performance in the same dairy herd population for 14 yr, accounting for other factors that modulate that association, such as milk production of a cow within the herd and her parity number.

Therefore, the first objective of the present study was to estimate the association of SCC with milk yield in grazing dairy cows of different levels of milk production. Our working hypothesis was that SCC is negatively associated with milk yield and that this association varies with parity and level of productivity, and it varies among herds in grazing dairy cows. The second objective was to assess the associations of the evolution and the severity of SCC with insemination and conception risks in grazing dairy cows. Our hypothesis was that the evolution and the severity of SCC are negatively associated with the reproductive performance in grazing dairy cows.

MATERIALS AND METHODS

Reference Population

Argentine dairy industry involves 1,580,000 dairy cows belonging to 10,400 dairy herds producing 11 billion kg/yr. Providing there is a high variability in herd size, 85 to 95% of them have 200 to 300 ha, with an average of 1.32 cow/ha. Milk yield by herd is also variable, given that the top 10% of farms produce 35% of national production. The predominant system is pastoral-based with energy and protein supplementation. In the last 2 decades, direct grazing has partially been replaced by conserved bulky forages and accompanied by an increase in the amount of energy supplementation. The preponderance of pastoral-based systems determines the seasonality of milk yield and the high variability of SCC across herds due to rains and associated mud. The average of SCC by year ranges from 350,000 up to 425,000 SCC/mL (FunPEL, 2014). Regarding the adoption of reproductive biotechnologies, a study involving 190 dairy herds found that 83% of herds have continuous service, 64% of them uses AI, from which 60% performed timed AI and 40% use visual heat detection. Finally, it was found that 29% of the AI were with sexed semen (Gastaldi et al., 2018). In our previous study, involving 657,968 lactations from 677 herds, we found that 50% of the herds had a pregnancy rate by 100 DIM over 31% from 2001 to 2006, and 27% from 2007 to 2012. Also, 50% of the herds had an average 305-d milk yield of 6,656 kg from 2001 to 2006, and 7,557 kg from 2007 to 2012 (Rearte et al., 2018).

Study Data Set

A retrospective longitudinal study was conducted using a data set including dairy herds from the Province of Buenos Aires, Argentina. Production, reproduction, and health records were periodically gathered by the official dairy herd improvement association (Association of Dairy Milk Check Entities from the Pampa Region) following the governmental normative (ACHA, 2018) complying the rules of International Committee for Animal Recording (ICAR). Data for all the lactations started between January 1, 2000, and December 31, 2014, that included periodic measures (30 or 40 d apart) of milk yield and fat percentage, protein percentage, and SCC were extracted from commercial software (Protambo Master 4.0, DIRSA SA) and centralized into a unique database (1,930,376 lactations from 867 herds). The official reproductive data included the dates of service, positive pregnancy diagnosis, and calving (ACHA, 1981). Reproductive data fulfilling the requirements of "calf registry" that is a working traceability system having individual identification, registration, and official certification of the offspring from the different dairy breeds used in Argentina following the guidelines of the international livestock organizations (World Holstein Friesian Federation, International Committee for Animal Recording, Interbull).

Variable Operationalization and Statistical Analysis

Association of SCC with Reproduction. A hazard regression model was fitted to estimate the insemination rate by 200 DIM (PROC PHREG, SAS 9.4, SAS Institute Inc.). In model 1, lactations having a service <40 DIM were left-censored, those culled or died were right-censored on the day of the respective event, and those having a last service >200 DIM were right censored at 200 DIM. The services of each lactation were considered as time-dependent repeated measurements by usign the counting process style of input. Included fixed predictors were: category of SCC (<150K or >150K) as a time-dependent variable by using a counting process (Allison, 1995); the number of services (first to fourth), DIM, parity, calving season, and calving year. The Efron approximation was used for handling ties in the data. The statistical significance of each independent variable was tested with a Wald test, with a robust sandwich estimate (Lin and Wei, 1989) to correct the dependence between repeated events (services) within lactation (a single origin for all services was defined). The correlation between Schoenfeld residual and time was used to test the assumption of proportionality.

Two multilevel logistic models (PROC GLIMMIX, SAS 9.4) were built to assess the odds for conception in each of the first 4 services per lactation. In model 2 the first SCC record measured within 43 d before service, and a second one measured within 30 d after service were used to define the evolution of SCC by using a 150,000 SCC/mL threshold as follows: healthy, both SCC record <150,000 SCC/mL; new case, first SCC record <150,000 SCC/mL and second ≥150,000 SCC/mL; cured, first SCC record ≥150,000 SCC/mL and second <150,000 SCC/mL; chronic, both SCC record ≥150,000 SCC/mL. Other fixed predictors included in the model were the number of services (first to fourth), the interaction of evolution of SCC with the number of services, DIM, parity (1, 2, and ≥3), calving season [summer (December 21 to March 20), autumn (March 21 to June 20), winter (June 21 to September 20), and spring (September 21 to December 20)], calving year (2000–2014) and herd (n = 580). In model 3, chronic SCC (SCC record having >150,000 SCC/mL 43 d before and 30 d after service) were classified according to the severity of SCC record measured 30 d after the service as follows: mild, SCC was between 150,000 and 400,000 SCC/mL; moderate, SCC was between 400,000 and 1,000,000 SCC/mL; severe, SCC was ≥1,000,000 SCC/mL. The interaction of severity of SCC with the number of services was included in the model, and all others fixed predictors were kept the same as in model 2. The random effect of lactation was included in the model to account for the correlation among services within lactation. Variance at the service level was considered as $\pi^2/3$ ($\pi = 3.1416$), based on interpreting the binary variable conception (yes or no) as the result of an underlying latent process with a continuous logistic distribution (Snijders and Bosker, 2012). Except for evolution and severity of SCC, the number of services and their interactions was forced to remain in the final model. All the variables included in the final model were selected following a backward process where they remain in the model if $P \leq 0.05$.

Lactations should meet all the following reproductive criteria to be included in the study: having at least one AI recorded; cows with a positive pregnancy diagnostic must have a subsequent calving record; and, if new calving took place, the interval between the last insemination and the new calving must be between 260 and 290 d. To be included in the insemination rate analysis (model 1), lactations must have at least one SCC record every 40 d until 200 DIM; and, finally, to be included in the conception risk analysis (models 2 and 3), lactations must have at least one SCC record 43 d before service and a second one 30 d after the service. Also, a herd-year effect was included in the analysis if at least 50% of their lactations fulfilled the previous requirements. In short, a set having 432,432 lactations from 769 herds were included in the analysis of insemination rate, and 802,066 services from 580 herds were included in conception risk analysis (Figure 1A,B).

Association of SCC with Milk Yield Two linear multilevel models (R studio; lme package) were fitted for parity numbers (first, second, and third or more) to assess the association of SCC with milk yield. Model 4 estimated the associations of daily milk yield with the following fixed predictors: linear score of daily SCC (LS-SCC); herd-year milk production quartile [(**MPQ**, estimated by using the milk yield lactation average

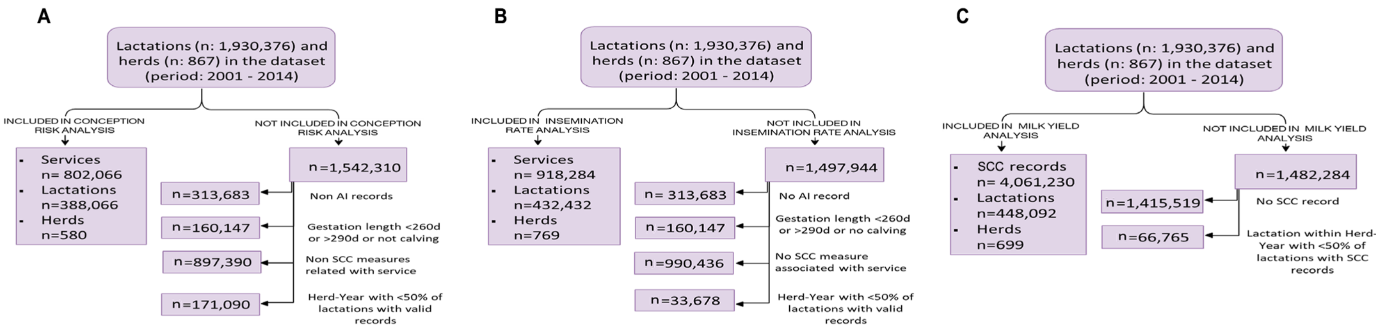

Figure 1. CONSORT diagram that describes the number of lactations included in conception risk analysis (A), insemination rate analysis (B), and milk yield analysis (C), and the number of lactations excluded from each analysis by exclusion criteria.

and categorizing it by quartiles within herd-year (top, upper middle, lower middle, bottom)]; the interaction between LS-SCC and MPQ; DIM; DIM^2; calving season; and calving year (2000–2014). The first-order autoregressive correlation structure was defined at the second level (repeated measures within lactations), and herd-year was defined at the third random level. Model 5 estimated the associations of daily milk yield with 11 SCC classes (from 0 to ≥1,000,000 SCC/mL, each 100,000 SCC/mL); DIM; DIM^2; calving season; and calving year. Random effects were defined as in model 4. The linear, cubic and quadratic relationship between SCC classes and daily milk yield were estimated. The coefficients for contrast effect were estimated with Proc IML (SAS 9.4).

Lactations must have on average one SCC measure every 40 d to be included in the study, and the herd-year was included if at least 50% of their lactations fulfilled such requirement. There were 4,061,230 daily measures of milk and SCC, belonging to 448,041 lactations from 699 herds, that could be included in the analysis (Figure 1C). Because of operational reasons for each lactation group, a subsample of 29.830 lactations (208,810 milk and SCC daily measures) belonging to 159 herds were selected to fit models 4 and 5. A random multistage sampling method was performed to select herds (n = 159) and lactations within selected herds (n = 190) for each lactation group. This sample size was estimated with a 95% confidence and 80% of power in both fixed cow predictors and random herd predictors to detect an effect on milk yield of z = 0.05, if all predictors included in the model accounted for 45% of milk yield, that remaining variability was explained in a ratio 2:1 at cow-1 and herd-2 levels, and if the correlation structure between cow levels variables was uniformly high (70%). The PintT software was used to estimate sample size (Snijders and Bosker, 1993).

RESULTS

Association of SCC with Reproduction

The results of model 1 are shown in Table 1. The daily risk of receiving a service by 200 DIM was associated with SCC, given that cows having more than 150,000 SCC/mL (n SCC measures = 1,203,665) have 2.7% (P < 0.001) lower hazard than cows having less than 150,000 SCC/mL (n SCC measures = 595,634). Parity, calving season, and calving year were also associated with the hazard of service, given that multiparous cows, cows calving in fall, and cows calving in the last years of study had a higher daily risk of receiving a service.

The results of model 2 assessing the odds for conception are shown in Table 2. Conception risk was associated with the category of SCC, the number of services, and their interaction (P < 0,001). The negative association of evolution of SCC with the odds for conception decreased with service number. The odds for conception at first service in cured, new case, and chronic cows were 7.9, 13.4, and 15.8% lower than in healthy cows, respectively. Whereas, the odds for conception at fourth service decreased 4.9, 9.3, and 8.6% in cured, new case, and chronic cows compared with healthy cows. Other predictors included in the final model also significantly affected conception rates: the DIM at service (AI), the primiparous cows, summer calving cows, and cows calved in early years of study who had larger odds of conception.

The results of model 3 are shown in Table 3. The severity of the mastitis was negatively associated with the odds for conception. Also, the interaction of severity by service number was significant (P < 0,001). The rates for conception at first service were 9.8, 16.3, and 29.1% lower for mild, moderate, and severe cows than in healthy cows. In contrast, the odds for conception at the fourth service were 6.3, 8.0, and 15.3% lower in mild, moderate, and severe cows than in healthy cows. This negative association was observed in all service number, but in the case of third and fourth services it was not significant.

Association of SCC with Milk Yield

Results of model 4 are shown in Tables 4, 5, and 6 for first-, second-, and third-lactation cows, respectively, and in Figure 2. Milk yield was associated with LS-SCC, given that an increase of one point of LS-SCC is accompanied by a daily milk yield decrease of 0.349, 0.539, and 0.676 kg for first-, second-, and third-lactation cows, respectively. In all these models, the interaction of LS-SCC by MPQ was associated with daily milk yield, given that in first calving cows, the deleterious effect of LS-SCC is even more negative in lower MPQ; and in second- and third-lactation cows, the estimated effect of LS-SCC is less negative in lower MPQ. In fact, first-parity cows have no difference in milk loss between the top and bottom MPQ, whereas second-parity cows in, the top quartile lost 15.5% more milk than those in the bottom quartile [a unit of increase in LS-SCC in top quartile was accompanied by a milk loss of 539 g (LSM = −0.539) vs. 455 g (LSM = −0.539 + 0.084) of milk loss in the bottom quartile]. Finally, in third-parity cows, these losses were 22.7% higher when the same comparison is performed [a unit of increase in LS_SCC at top quartile was accompanied by a milk loss of 676 g (LSM = −0.676) vs. 522 g (LSM = −0.676 + 0.154) of milk loss in bottom quartile cows (Figure 2)]. Also, the intraclass correlation showed that the herd level represented between 31.1 and 36.0% of the variability in daily milk yield depending on parity number.

Results of model 5 are shown in Figure 3. The negative slope of milk yield through SCC-Q was similar for second and third parity cows, whereas, for first lactation cows, the slope was less pronounced. Linear, quadratic, and cubic contrasts were statistically significant in the 3 lactation groups.

Table 1. Proportional hazard regression model to assess the effect of the category of SCC, service number, parity, calving season, and calving year on the daily risk of receiving service at 200 DIM, from 432,432 lactations belonging to 769 Argentinean dairy herds for 14 years (2000–2014)

Variable	Hazard ratio	95% CI	*P*-value
C_SCC[1]			
<150 k	Referent		
>150 k	0.973	0.959– 0.986	<0.001
Service number			
First	Referent		
Second	0.907	0.878–0.937	<0.001
Third	0.915	0.876–0.956	<0.001
Fourth	0.930	0.888–0.975	0.002
Parity			
1	Referent		
2	1.075	1.060–1.092	<0.001
3	1.109	1.089–1.130	<0.001
≥4	1.100	1.076–1.125	<0.001
Calving season			
Fall	Referent		
Winter	0.940	0.926–0.954	<0.001
Spring	0.826	0.804–0.849	<0.001
Summer	0.888	0.867–0.910	<0.001
Calving year			
2000	0.746	0.696–0.799	<0.001
2001	0.757	0.699–0.819	<0.001
2002	0.696	0.644–0.752	<0.001
2003	0.733	0.690–0.779	<0.001
2004	0.728	0.682–0.777	<0.001
2005	0.762	0.712–0.815	<0.001
2006	0.768	0.726–0.812	<0.001
2007	0.781	0.739–0.825	<0.001
2008	0.773	0.733–0.816	<0.001
2009	0.807	0.768–0.848	<0.001
2010	0.800	0.765–0.837	<0.001
2011	0.786	0.753–0.821	<0.001
2012	0.786	0.754–0.819	<0.001
2013	0.803	0.772–0.836	<0.001
2014	Referent		

[1]C_SCC: category of SCC (>150,000 vs. <150,000 SCC/mL).

DISCUSSION

In agreement with our working hypothesis, higher levels of SCC and their temporal relationship with the moment of service are associated with a decrease in the risk for conception in grazing dairy cows. This negative effect is even more significant in cows having high SCC within 30 d after their service date (such as new cases and chronic groups) and, it is also strongly associated with the severity of mastitis. Also, the observed adverse effects of SCC tended to decrease with service number, which is expected because, in the subpopulation of cows that fail to get pregnant, there could be other potential variables explaining their poor fertility.

In our study, the conception risk in cows having high SCC before service (such as cured and new case groups) were less affected than in a previous report (Lavon et al., 2011a), but the negative effect detected in severe cases of mastitis (chronic group) were almost the same. Lavon et al. (2011a) showed that cured, new case, and chronic groups had 7, 16, and 20% [proportion of pregnant cows among those inseminated (**CR**) = 39.4, 36.6, 32.9, and 31.5%] lower conception risk than healthy cows, whereas on our study conception risks were 4.0, 6.2, and 13.0% lower (CR = 33.6, 32.2, 31.5, and 29.0%) than in healthy cows. For example, the probability of conception in severe chronic cases was 24.6% lower (CR = 29.7 vs. 39.4%) than in healthy cows (Lavon et al.,

Table 2. Logistic regression model assessing the effect of the evolution of SCC, the number of services, and their interaction on the odds of conception adjusted by parity, DIM, calving season, and calving year (data not shown) for 802,066 services from 388,066 lactations belonging to 580 Argentinean dairy herds for 14 years (2000–2014)

Variable	SCC category[1]	Services (n)	Conception (%)	Odds ratio	95% CI
First service	Healthy	179,772	33.6	Referent	
	Cured	52,972	32.2	0.921	0.902–0.941
	New case	54,288	31.5	0.866	0.848–0.884
	Chronic	74,657	29.2	0.842	0.826–0.859
Second service	Healthy	115,048	32.6	Referent	
	Cured	31,978	30.5	0.920	0.870–0.973
	New case	36,824	30.0	0.891	0.844–0.941
	Chronic	52,618	29.8	0.880	0.838–0.925
Third service	Healthy	62,913	30.8	Referent	
	Cured	18,356	29.4	0.939	0.881–1.000
	New case	21,166	28.6	0.904	0.850–0.962
	Chronic	32,316	28.8	0.912	0.863–0.963
Fourth service	Healthy	31,136	28.1	Referent	
	Cured	9,479	27.1	0.951	0.880–1.027
	New case	10,986	26.1	0.907	0.841–0.979
	Chronic	17,557	26.3	0.914	0.856–0.977
Lactation random effect				0.233	0.233–0.234

[1]SCC categories: first SCC record measured within 43 d before service, and a second one measured within 30 d after service were used to define the evolution of SCC by using a 150,000 SCC/mL threshold as follows: healthy, both SCC records <150,000 SCC/mL; new case, first SCC record <150,000 SCC/mL and second ≥150,000 SCC/mL; cured, first SCC record ≥150,000 SCC/mL and second <150,000 SCC/mL; chronic, both SCC records ≥150,000 SCC/mL.

2011a), whereas in our study, it was 22.3% lower (CR = 26.1 vs. 33.6%). This finding could support the use of specific treatments with nonsteroidal inflammatory drugs such as meloxicam on recently inseminated cows having more than 1,000,000 SCC/mL as suggested by McDougall et al. (2016).

From the above-mentioned findings, we could propose that the negative effect of SCC on fertility seems more related to a reduction in the risk for conception than on the daily risk for service where it had marginal importance from a practical point of view (a reduction of 2.7%).

Table 3. Logistic regression model assessing the effect of severity of SCC, the number of services, and their interaction in the odds of conception adjusted by parity, DIM, calving season, and calving year (data not shown) for 566,017 services from 318,705 lactations belonging to 557 Argentinean dairy herds for 14 years (2000–2014)

Variable	SCC severity[1]	Service (n)	Conception (%)	Odds ratio	95% CI
First service	Healthy	179,772	33.6	Referent	
	Mild	39,315	31.0	0.902	0.881–0.925
	Moderate	18,241	29.4	0.837	0.808–0.866
	Severe	17,101	26.1	0.709	0.683–0.736
Second service	Healthy	115,048	32.6	Referent	
	Mild	27,587	30.9	0.931	0.875–0.990
	Moderate	12,984	28.3	0.818	0.759–0.934
	Severe	12,047	27.5	0.787	0.717–0.865
Third service	Healthy	62,913	30.8	Referent	
	Mild	16,924	29.9	0.961	0.897–1.029
	Moderate	8,078	28.8	0.912	0.827–1.006
	Severe	7,314	26.0	0.794	0.715–0.882
Fourth service	Healthy	31,136	28.2	Referent	
	Mild	9,227	26.8	0.937	0.862–1.018
	Moderate	4,400	26.4	0.920	0.820–1.034
	Severe	3,930	24.9	0.847	0.748–0.960
Lactation random effect				0.999	0.997–1.001

[1]SCC severity: chronic SCC were classified according to the severity of SCC record measured 30 d after the service as follows: mild, SCC between 150,000 and 400,000 SCC/mL; moderate, SCC between 400,000 and 1,000,000 SCC/mL; severe, SCC ≥1,000,000 SCC/mL; healthy, both SCC records <150,000 SCC/mL.

Table 4. Multilevel linear model to estimate daily milk yield in primiparous cows from fixed effects of the linear score of SCC, milk production quartile, and their interaction for 29,830 lactations belonging to 159 Argentinean dairy herds for 14 years (2000–2014)

Predictor	Level	Mean (SE)	95% CI	*P*-value
Intercept		32.365 (0.235)	31.904 to 32.826	<0.001
LS-SCC[1]		−0.349 (0.009)	−0.367 to −0.331	<0.001
MPQ[2]	Top	Referent		
	Upper middle	−4.825 (0.046)	−4.915 to −4.735	<0.001
	Lower middle	−9.226 (0.046)	−9.316 to −9.136	<0.001
	Bottom	−14.370 (0.072)	−14.511 to −14.229	<0.001
LS-SCC × MPQ	at Upper middle	−0.058 (0.012)	−0.082 to −0.034	<0.001
	at Lower middle	−0.026 (0.011)	−0.048 to −0.004	0.018
	at Bottom	−0.017 (0.017)	−0.050 to 0.016	0.371
Herd-residual[3]		14.695 (1.692)	11.379 to 18.011	
Cow-residual		14.002 (0.170)	13.669 to 14.335	
Residual		13.999 (0.043)	13.915 to 14.083	

[1]LS-SCC: linear score of SCC.

[2]MPQ: milk production quartile (top, upper middle, lower middle, bottom). Other included factors were calving season, calving year, DIM, and DIM^2 (parameters not shown).

[3]ICC = [Herd-residual/(Herd-residual + Cow-residual + Residual)] × 100 = 34.4%. Intercept random effects were estimated at herd and cow level (first-order autoregressive correlation). Others covariables included in the model were calving season, year of calving, DIM, and DIM^2.

Models assessing milk losses (models 4, 5, and 6) showed that the interaction of LS-SCC by MPQ is associated with daily milk yield, but that association has neither the same direction nor effect size in the different parity groups.

Previous work reported milk yield losses when comparing 200,000 SCC/mL with the baseline of 50,000 SCC/mL range from −0.28 to −0.8 kg/d in first parity cows, from −0.61 to −1.4 kg in second parity cows, and from −0.63 to −2.41 kg in third-parity cows (Boland et al., 2013). Our estimated parameters agree with these reported ranges, given that losses go from −0.69 to −0.81 kg in first parity cows, from −1.07 to −1.24 kg in second parity cows, and from −1.35 to −1.6 kg in third-parity cows, depending on the quartile of milk production. We found a higher variability among herds in milk yield (ICC = 31.1–36% depending on parity) than that reported by Boland et al. (2013) in Ireland, where they reported an ICC of 29% at the herd level. This result has practical importance for extrapolating the parameters estimated in this study. They should be used as mean population values but should not be used for making predictions for cows belonging to a particular herd.

The finding that the relationship between SCC and daily milk yield is nonlinear (e.g., quadratic or cubic function; Figure 3) highlighted the need for log-transformation of SCC when fitting linear models. In

Table 5. Multilevel linear model to estimate daily milk yield in second-calving cows from fixed effects of the linear score of SCC, milk production quartile, and their interaction for 29,830 lactations belonging to 159 Argentinean dairy herds for 14 years (2000–2014)

Predictor	Level	Mean (SE)	95% CI	*P*-value
Intercept		40.461 (0.206)	40.057 to 40.865	<0.001
LS-SCC[1]		−0.539 (0.010)	−0.559 to 0.519	<0.001
MPQ[2]	Top	Referent		
	Upper middle	−5.714 (0.057)	−5.826 to 5.602	<0.001
	Lower middle	−9.668 (0.060)	−9.786 to 9.550	<0.001
	Bottom	−14.624 (0.060)	−14.742 to 14.506	<0.001
LS-SCC × MPQ	at Upper middle	0.009 (0.014)	−0.018 to 0.036	0.544
	at Lower middle	0.061 (0.014)	0.034 to 0.088	<0.001
	at Bottom	0.084 (0.015)	0.055 to 0.113	<0.001
Herd-residual[3]		20.997 (2.436)	16.222 to 25.771	
Cow-residual		23.015(0.264)	22.497 to 23.532	
Residual		19.355 (0.059)	19.239 to 19.470	

[1]LS-SCC: linear score of SCC.

[2]MPQ: milk production quartile (top, upper middle, lower middle, bottom), Other included factors were calving season, calving year, DIM, and DIM^2 (parameters not shown).

[3]ICC = [Herd-residual/(Herd-residual + Cow-residual + Residual)] × 100 = 33.1%. Intercept random effects were estimated at herd and cow level (first-order autoregressive correlation).

Table 6. Multilevel linear model to estimate daily milk yield in cows of third or greater calving, from fixed effects of the linear score of SCC, production quartile, and their interaction for 29,830 lactations belonging to 159 Argentinean dairy herds for 14 years (2000–2014)

Predictor	Level	Mean (SE)	CI 95%	*P*-value
Intercept		42.566 (0.424)	41.735 to 43.397	<0.001
LS-SCC[1]		−0.676 (0.017)	−0.709 to 0.643	<0.001
MPQ[2]	Top	Referent		
	Upper middle	−6.076 (0.110)	−6.292 to −5.860	<0.001
	Lower middle	−9.824 (0.117)	−10.053 to −9.595	<0.001
	Bottom	−14.502 (0.127)	−14.751 to 14.253	<0.001
LS-SCC × MPQ	at Upper middle	0.095 (0.024)	0.048 to 0.142	<0.001
	at Lower middle	0.134 (0.025)	0.085 to 0.183	<0.001
	at Bottom	0.154 (0.025)	0.105 to 0.203	<0.001
Herd-residual[3]		23.902 (2.763)	18.486 to 29.317	
Cow-residual		18.433 (0.260)	17.923 to 18.942	
Residual		23.988 (0.071)	23.848 to 24.127	

[1]LS-SCC: linear score of SCC.

[2]MPQ: milk production quartile (top, upper middle, lower middle, bottom). Other included factors were calving season, calving year, DIM, and DIM^2 (parameters not shown).

[3]ICC = [Herd-Residual/(Herd-Residual + Cow-Residual + Residual)] × 100 = 36%. Intercept random effects were estimated at Herd and Cow level (first-order autoregressive correlation).

addition, in Figure 3, we can also observe that milk losses begin with relatively low SCC values (≤100,000 SCC/mL), and that agrees with estimations obtained in models 4, 5, and 6, where the highest milk yield losses occurred in older cows.

The main strengths of the present study are the huge data set assessed involving the records of 1,930,376 lactations from 867 dairy herds obtained for 14 yr and, as far as we know, this is the first large-scale study evaluating the association of SCC with indicators of both productive and reproductive performance in dairy cows at the same time. The main limitations are related to the properties of retrospective observational studies, that as they are run on secondary sources of information, it is not possible to assess full cause-effect relationships. In this sense, our data set had neither record about diseases (e.g.; diagnosis and treatment of clinical mastitis) nor the reproductive management of

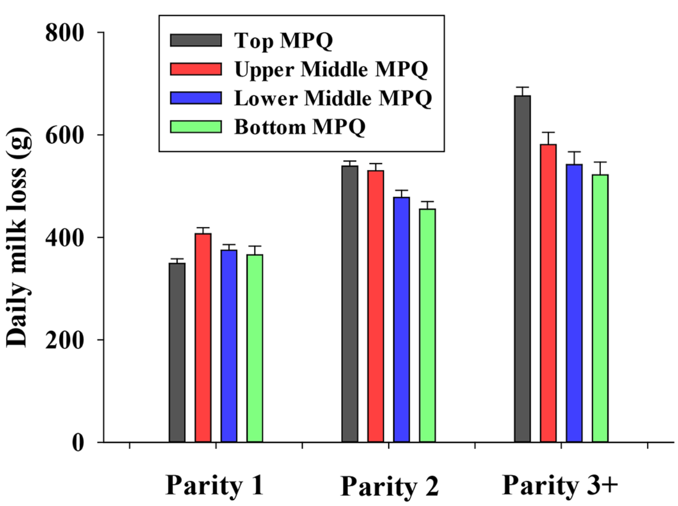

Figure 2. Least squares means (±SE) of daily milk loss estimated with a multilevel linear model with fixed effects of the linear score of SCC, the within-herd milk production quartile (MPQ), and their interaction for 29,830 lactations belonging to 159 Argentinean dairy herds for 14 years (2000–2014). Other included factors were calving season, calving year, DIM, and DIM^2 (parameters not shown). The random effects were estimated at the herd and cow levels.

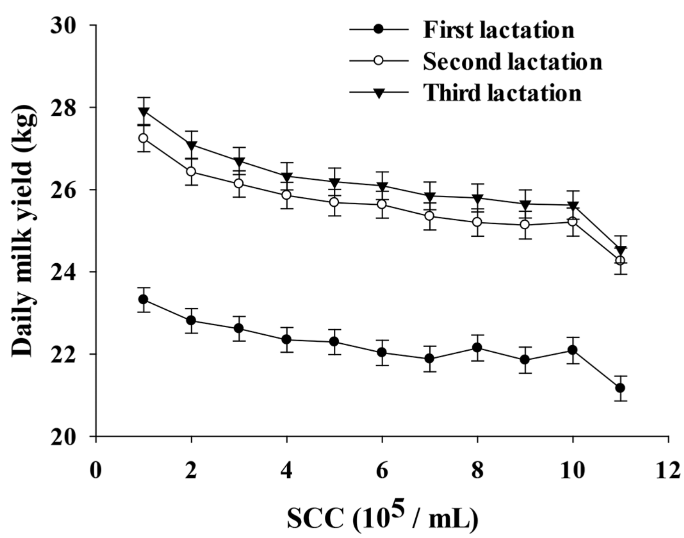

Figure 3. Least squares means (±SE) of daily milk yield estimated with a multilevel linear model with fixed effects of a class of SCC (every 100,000 SCC/mL), parity, and their interaction for 29,830 lactations belonging to 159 Argentinean dairy herds for 14 years (2000–2014). Other included factors were calving season, calving year, DIM, and DIM^2 (parameters not shown). The random effects were estimated at the herd and cow levels. Contrasts of linear, quadratic, and cubic functional relationships were significant with $P < 0.001$.

the dairy cows. Also, the relationship between SCC and milk yield was assessed with a cross-sectional analysis because the frequency of milk checks (monthly) does not allow a precise evaluation of their temporal association.

CONCLUSIONS

The SCC is negatively associated with the risk for conception and with daily milk yield in grazing dairy cows. The risk for conception depends on the temporal association of the SCC with the service date and the severity of mastitis. Lower milk yield is influenced by milk production quartile, parity and the severity of mastitis.

ACKNOWLEDGMENTS

The authors thank the Association of the Pampeana Regional of Milk Check Entities (ARPECOL), and National Commission for Scientific and Technological Research (CONICET) for their financial support and for providing scholarships. Contributors R.R., R.D.S., I.L.M. and M.J.G. designed the study and developed the protocol and analysis plan. R.R. and S.C. cleaned and analyzed the data. R.R., R.D.S. and M.J.G. drafted the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. R.R. and M.J.G. are the guarantors. The data presented in this study are available as restricted-access in Mendeley Data at https://doi.org/10.17632/d8kgk57b9h.3. The authors have not stated any conflicts of interest.

REFERENCES

ACHA. 1981. Regulations. [in Spanish] Accessed Nov. 11, 2021. https://www.acha.org.ar/index.php/empresa2/empresa-servicios/reglamentos.

ACHA. 2018. Manual of procedures of the milk control system. [in Spanish] Accessed Feb. 13, 2021. https://www.ocla.org.ar/contents/news/details/13361354-manual-de-procedimientos-del-sistema-de-control-lechero.

Allison, P. D. 1995. Survival Analysis Using the SAS System: A Practical Guide. SAS Institute.

Barker, A. R., F. N. Schrick, M. J. Lewis, H. H. Dowlen, and S. P. Oliver. 1998. Influence of clinical mastitis during early lactation on reproductive performance of Jersey cows. J. Dairy Sci. 81:1285–1290. https://doi.org/10.3168/jds.S0022-0302(98)75690-5.

Boland, F., L. O'Grady, and S. J. More. 2013. Investigating a dilution effect between somatic cell count and milk yield and estimating milk production losses in Irish dairy cattle. J. Dairy Sci. 96:1477–1484. https://doi.org/10.3168/jds.2012-6025.

Chebel, R. C., J. E. P. Santos, J. P. Reynolds, R. L. A. Cerri, S. O. Juchem, and M. Overton. 2004. Factors affecting conception rate after artificial insemination and pregnancy loss in lactating dairy cows. Anim. Reprod. Sci. 84:239–255. https://doi.org/10.1016/j.anireprosci.2003.12.012.

Dürr, J. W., R. I. Cue, H. G. Monardes, J. Moro-Mendez, and K. M. Wade. 2008. Milk losses associated with somatic cell counts per breed, parity and stage of lactation in Canadian dairy cattle. Livest. Sci. 117:225–232. https://doi.org/10.1016/j.livsci.2007.12.004.

Fuenzalida, M. J., P. M. Fricke, and P. L. Ruegg. 2015. The association between occurrence and severity of subclinical and clinical mastitis on pregnancies per artificial insemination at first service of Holstein cows. J. Dairy Sci. 98:3791–3805. https://doi.org/10.3168/jds.2014-8997.

FunPEL (Fundación para la Promoción y el Desarrollo de la Cadena Láctea Argentina). 2014. Lechería Argentina Anuario 2014. Fundación para la Promoción y el Desarrollo de la Cadena Láctea Argentina. Accessed Nov. 20, 2021. https://produccionbovina.files.wordpress.com/2017/08/anuario-de-la-lecherc3ada-argentina-2014.pdf.

Furman, O., G. Leitner, Z. Roth, Y. Lavon, S. Jacoby, and D. Wolfenson. 2014. Experimental model of toxin-induced subclinical mastitis and its effect on disruption of follicular function in cows. Theriogenology 82:1165–1172. https://doi.org/10.1016/j.theriogenology.2014.08.002.

Gastaldi, L. B., A. R. Centeno, G. M. Litwin, M. Maekawa, M. R. Marino, M. L. Moretto, A. Cuatrin, and P. L. Engler. 2018. Lechería pampeana resultados del ejercicio 2016–2017: Información para productores. http://hdl.handle.net/20.500.12123/2584.

Giordano, J. O., A. S. Kalantari, P. M. Fricke, M. C. Wiltbank, and V. E. Cabrera. 2012. A daily herd Markov-chain model to study the reproductive and economic impact of reproductive programs combining timed artificial insemination and estrus detection. J. Dairy Sci. 95:5442–5460. https://doi.org/10.3168/jds.2011-4972.

Hagnestam-Nielsen, C., and S. Østergaard. 2009. Economic impact of clinical mastitis in a dairy herd assessed by stochastic simulation using different methods to model yield losses. Animal 3:315–328. https://doi.org/10.1017/S1751731108003352.

Halasa, T., M. Nielen, A. P. W. De Roos, R. Van Hoorne, G. de Jong, T. J. G. M. Lam, T. van Werven, and H. Hogeveen. 2009. Production loss due to new subclinical mastitis in Dutch dairy cows estimated with a test-day model. J. Dairy Sci. 92:599–606. https://doi.org/10.3168/jds.2008-1564.

Hand, K. J., A. Godkin, and D. F. Kelton. 2012. Milk production and somatic cell counts: A cow-level analysis. J. Dairy Sci. 95:1358–1362. https://doi.org/10.3168/jds.2011-4927.

Herath, S., E. J. Williams, S. T. Lilly, R. O. Gilbert, H. Dobson, C. E. Bryant, and I. M. Sheldon. 2007. Ovarian follicular cells have innate immune capabilities that modulate their endocrine function. Reproduction 134:683–693. https://doi.org/10.1530/REP-07-0229.

Hertl, J. A., Y. H. Schukken, F. L. Welcome, L. W. Tauer, and Y. T. Gröhn. 2014. Effects of pathogen-specific clinical mastitis on probability of conception in Holstein dairy cows. J. Dairy Sci. 97:6942–6954. https://doi.org/10.3168/jds.2014-8203.

Hortet, P., F. Beaudeau, H. Seegers, and C. Fourichon. 1999. Reduction in milk yield associated with somatic cell counts up to 600,000 cells/mL in French Holstein cows without clinical mastitis. Livest. Prod. Sci. 61:33–42. https://doi.org/10.1016/S0301-6226(99)00051-2.

Hudson, C. D., A. J. Bradley, A. J. Breen, and M. J. Green. 2015. Dairy herd mastitis and reproduction: Using simulation to aid interpretation of results from discrete time survival analysis. Vet. J. 204:47–53. https://doi.org/10.1016/j.tvjl.2015.01.024.

Hudson, C. D., A. J. Bradley, J. E. Breen, and M. J. Green. 2012. Associations between udder health and reproductive performance in United Kingdom dairy cows. J. Dairy Sci. 95:3683–3697. https://doi.org/10.3168/jds.2011-4629.

Krpalkova, L., V. E. Cabrera, J. Kvapilik, and J. Burdych. 2016. Associations of reproduction and health with the performance and profit of dairy cows. Agric. Econ. Czech. 62:385–394. https://doi.org/10.17221/176/2015-AGRICECON.

Lavon, Y., E. Ezra, G. Leitner, and D. Wolfenson. 2011a. Association of conception rate with pattern and level of somatic cell count elevation relative to time of insemination in dairy cows. J. Dairy Sci. 94:4538–4545. https://doi.org/10.3168/jds.2011-4293.

Lavon, Y., G. Leitner, U. Moallem, E. Klipper, H. Voet, S. Jacoby, G. Glick, R. Meidan, and D. Wolfenson. 2011b. Immediate and carryover effects of Gram-negative and Gram-positive toxin-induced mastitis on follicular function in dairy cows. Theriogenology 76:942–953. https://doi.org/10.1016/j.theriogenology.2011.05.001.

Lin, D. Y., and L. J. Wei. 1989. The robust inference for the Cox proportional hazards model. J. Am. Stat. Assoc. 84:1074–1078. https://doi.org/10.2307/2290085.

McDougall, S., E. Abbeloos, S. Piepers, A. S. Rao, S. Astiz, T. van Werven, J. Statham, and N. Pérez-Villalobos. 2016. Addition of meloxicam to the treatment of clinical mastitis improves subsequent reproductive performance. J. Dairy Sci. 99:2026–2042. https://doi.org/10.3168/jds.2015-9615.

Pinedo, P. J., P. Melendez, J. A. Villagomez-Cortes, and C. A. Risco. 2009. Effect of high somatic cell counts on reproductive performance of Chilean dairy cattle. J. Dairy Sci. 92:1575–1580. https://doi.org/10.3168/jds.2008-1783.

Rearte, R., S. J. LeBlanc, S. G. Corva, R. L. de la Sota, I. M. Lacau-Mengido, and M. J. Giuliodori. 2018. Effect of milk production on reproductive performance in dairy herds. J. Dairy Sci. 101:7575–7584. https://doi.org/10.3168/jds.2017-13796.

Ribeiro, E. S., G. Gomes, L. F. Greco, R. L. A. Cerri, A. Vieira-Neto, P. L. J. Monteiro Jr., F. S. Lima, R. S. Bisinotto, W. W. Thatcher, and J. E. P. Santos. 2016. Carryover effect of postpartum inflammatory diseases on developmental biology and fertility in lactating dairy cows. J. Dairy Sci. 99:2201–2220. https://doi.org/10.3168/jds.2015-10337.

Roth, Z., A. Dvir, D. Kalo, Y. Lavon, O. Krifucks, D. Wolfenson, and G. Leitner. 2013. Naturally occurring mastitis disrupts developmental competence of bovine oocytes. J. Dairy Sci. 96:6499–6505. https://doi.org/10.3168/jds.2013-6903.

Ruegg, P. L., and R. J. Erskine. 2014. Mammary Gland Health. Pages 1015–1043 in Large Animal Internal Medicine. 5th ed. Mosby Elsevier.

Santos, J. E., R. L. Cerri, M. A. Ballou, G. E. Higginbotham, and J. H. Kirk. 2004. Effect of timing of first clinical mastitis occurrence on lactational and reproductive performance of Holstein dairy cows. Anim. Reprod. Sci. 80:31–45. https://doi.org/10.1016/S0378-4320(03)00133-7.

Schrick, F. N., M. E. Hockett, A. M. Saxton, M. J. Lewis, H. H. Dowlen, and S. P. Oliver. 2001. Influence of subclinical mastitis during early lactation on reproductive parameters. J. Dairy Sci. 84:1407–1412. https://doi.org/10.3168/jds.S0022-0302(01)70172-5.

Snijders, T. A. B., and R. J. Bosker. 1993. Standard errors and sample sizes for two-level research. J. Educ. Stat. 18:237–259. https://doi.org/10.3102/10769986018003237.

Snijders, T. A. B., and R. J. Bosker. 2012. Multilevel Analysis: An Introduction to Basic and Advanced Multilevel Modeling. 2nd edition. Sage Publishers.

Vissio, C., D. A. Agüero, C. G. Raspanti, L. M. Odierno, and A. J. Larriestra. 2015. Pérdidas productivas y económicas diarias ocasionadas por la mastitis y erogaciones derivadas de su control en establecimientos lecheros de Córdoba, Argentina. Arch. Med. Vet. 47:7–14. https://doi.org/10.4067/S0301-732X2015000100003.

ORCIDS

R. Rearte https://orcid.org/0000-0003-1182-4454
S. G. Corva https://orcid.org/0000-0003-1898-4709
R. L. de la Sota https://orcid.org/0000-0002-9417-9560
I. M. Lacau-Mengido https://orcid.org/0000-0003-2547-3819
M. J. Giuliodori https://orcid.org/0000-0002-3235-3711