Preventive Veterinary Medicine 191 (2021) 105359

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

Clinical disease incidence during early lactation, risk factors and association with fertility and culling in grazing dairy cows in Uruguay

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ARTICLE INFO

Keywords:
Disease incidence
Dairy cow
Pasture based system
Early lactation

ABSTRACT

This paper aims to describe clinical disease incidence in early lactation and explore its association with fertility and culling in 13 commercial grazing dairy herds in Uruguay. Seven farms with less than 250 dairy cows considered small herds (SH) with a herd size average ± (SD) of 144 ± (56) cows and six farms with more than 500 cows considered large herds (LH) with a herd size average ± (SD) of 830 ± (239) cows were selected. Herd managers recorded health events during the first 90 days in milk in 5375 Holstein dairy cows [24.5% (n=1316) of them were primiparous cows, (PP)] during one year. Overall, 36.5% (n=1959) of the cows had at least one clinical health event between 1–90 days in milk. The cumulative incidences were 2.2% for twin birth and 4.9% for stillbirth. Cumulative incidence was 4.4% for retained placenta-metritis (RP-metritis), 27.6% for clinical mastitis and 5.0% for lameness. Our data showed that parity and herd size were risk factors for postpartum disease in grazing dairy herds. In PP cows, stillbirth incidence was higher than in multiparous (MP) cows (PP=6.9 ± 3.4, SD vs. MP=4.3 ± 2.6, SD), while in MP cows twin births (MP=2.7 ± 1.7, SD vs. PP=0.7 ± 2.7, SD), RP-metritis (MP=4.6 ± 3.9, SD vs. PP=3.8 ± 3.7, SD) and mastitis incidence (MP=30.9 ± 11.4, SD vs. PP=17.2 ± 13.9, SD) was higher. Clinical mastitis (LH=29.4 ± 9.6, SD vs. SH=19.1 ± 11.3, SD) and lameness incidence (LH=5.6 ± 1.9, SD vs. SH=2.3 ± 2.1, SD) was higher in large herds than in small herds. RP-metritis was increased by stillbirth (OR=4.4, 95 % CI=2.9–6.5) and twin birth (OR=2.8, 95 % CI=1.5–5.1). Diseases had a negative impact on time to first service and pregnancy rate and increased culling hazard rate. Disease incidence in early lactation was high and showed a wide variation among herds (10.4%–48.7%), which highlights the relevance of a herd health program prioritizing the early lactation disease control.

1. Introduction

It is well known that diseases (clinical and subclinical) can compromise animal welfare and lead to economic losses, increasing the risk of involuntary culling (Galligan, 2006; Kerslake et al., 2018), although few reports are available about postpartum clinical disease on grazing dairy herd. Disease has been responsible for higher number of open days (McDougall, 2001), decrease in milk quality and quantity and elevated costs related to treatments and replacement animals (Ingvartsen, 2006; Mulligan and Doherty, 2008). The risk for health problems is highest during the transition period in the lactating cow, especially in the first month after calving (Goff and Horst, 1997; LeBlanc et al., 2006) because of the negative energy balance (NEB) (Drackley, 1999) and depression of the immune system (Wells et al., 1977; Detilleux et al., 1995) that affects all cows. LeBlanc (2010) reported that between 30–50% of dairy cows suffered some type of disease during the transition period. Several studies also reported a strong association between diseases; for instance, cows with a stillbirth are at greater risk of retained placenta and metritis, while cows developing milk fever are at greater risk of abomasal displacement (Curtis et al., 1983; Oltenacu et al., 1990; Correa et al., 1993).

Most of the information related to health and disease in dairy cows has been generated in confinement systems. Studies comparing confinement and grazing systems consistently reported fewer clinical

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https://doi.org/10.1016/j.prevetmed.2021.105359
Received 8 October 2020; Received in revised form 12 April 2021; Accepted 13 April 2021
Available online 18 April 2021
0167-5877/

health problems in the latter (Goldberg et al., 1992; Washburn et al., 2002), although Sepúlveda Varas et al. (2015) reported high clinical and subclinical disease incidence even in grazing herds. This is relevant, since the consumer image of grazing cows is associated with animal welfare (Verkerk and Hemsworth, 2010), but the trend to increase farm size (Robbins et al., 2016) may increase disease incidence. According to Beggs et al. (2015), increasing herd size in grazing systems entails longer milking times, more time away from the paddock and longer walking distance, reducing animal welfare unless specific husbandry practices are implemented (Verkerk and Hemsworth, 2010). Indeed, a higher lameness prevalence (Flor and Tadich, 2008) were reported on larger dairy farms and also reduced bulk tank somatic cell counts was associated with smaller herds (McDougall, 2003). In confined systems, involuntary culling rate increased with herd size (Smith et al., 2000), which is related to animal welfare (McConnel, 2010) and lower dairy farm profitability (Armengol and Fraile, 2018).

Parity is also a well-known risk factor for some diseases (Ruprechter et al., 2018), as primiparous cows (PP) have a higher risk of metritis than multiparous cows (MP) (Sepúlveda Varas and Wittwer Menge, 2017). However, MP cows have a higher risk of milk fever, subclinical hypocalcemia, retained placenta and mastitis (Reinhardt et al., 2011; Suthar et al., 2013; Richardet et al., 2016; Ruprechter et al., 2018). The adaptation of PP cows to the transition period differs from MP cows because they have additional energy requirements for growth, in addition to the stress of the first calving and introduction to the milking parlour, among others (Eicher et al., 2007).

As mentioned before, health studies in dairy grazing systems are scarce (Sepúlveda Varas et al., 2015). Additionally, cow management in grazing systems is strongly influenced by climatic conditions; therefore, the risk factors affecting cows may also differ (Compton et al., 2007) from housed systems. Thus, this paper aims to describe the magnitude and variation of disease incidence during early lactation in commercial grazing dairy herds, and explore risk factors for disease and their association with fertility and culling.

2. Materials and methods

The experimental protocol was evaluated and approved by the Honorary Committee for Animal Experimentation in Uruguay (CHEA – UdelaR, Montevideo, Uruguay).

2.1. Dairy herd selection

A prospective cohort study was conducted in 13 commercial dairy herds located within a radius of 40 km around Florida, Uruguay (34°05′ S and 56°12′ W). Herd selection was based on convenience: the herds were required to have permanent professional advice (agronomist and veterinarian), and reliable health, reproductive and productive records. Seven dairy herds (numbered 1–7) were classified as small herds (SH), with an average (SD) herd size of 144 (±56), cows. Six were classified as large herds (LH) (numbered 8–13), with an average (SD) herd size of 830 (±239) cows. Dairy herds were visited every 20 days by the same veterinarian (the first author). A total number of 5375 Holstein dairy cows were included in this study. Descriptive information about productive indicators of the herds is presented in the Supplementary table.

2.2. Feeding and milking management

All the dairy herds used a mixed grazing system. Cows grazed all year round and were supplemented with grain-based concentrate and conserved forage (silage, haylage or hay). Mean kg of dry matter (DM)/cow/day throughout the year is shown in the supplementary table. The supplement, in particular the forages, varied according to pasture deficit. All small herds and farms 8, 9 and 13 fed concentrates in the milking parlour. The other large herds (farms 10, 11 and 12) fed concentrates exclusively in the partial mixed ration (PMR) at feed bunks. All cows were milked twice a day. Monthly test day was performed in 10 of the 13 dairy herds.

2.3. Reproductive management

The small herds had an all year round calving system while the large herds had a seasonal calving system (6–9 months) starting in autumn (February to April), except for herd 9, which had a split calving system [autumn and spring (August to October)]. Average rainfall for each season was 216 mm for autumn, 86 mm for winter, 75 mm for spring and 71 mm for summer. Relative to average temperature for each season was 17.5°C for autumn, 10°C for winter, 13°C for spring and 21°C for summer (INIA, 2021).

The voluntary waiting period varied according to each herd and averaged 44.6 (±8.0, SD) days. All dairy herds used artificial insemination (AI) with estrous detection, while dairy herds 8, 10 and 11 (LH) also used fixed time AI at the beginning of the mating period. Dairy herds 1, 3, 5, 7 and 12 used exclusively AI, the others combined AI and bulls. Pregnancy diagnosis was performed by the dairy herd veterinarian by transrectal palpation or ultrasonography 35–60 days after breeding. Breeding and pregnancy information up to 300 days in milk (DIM) was recorded.

2.4. Udder health management

All dairy herds used dry cow antibiotic therapy, and except for herd 6, all herds used post-milking teat dipping. Only herds 5, 8 and 9 used pre-milking disinfection and herds 2, 5, 7, 9, 10, 11 and 13 performed forestripping. Small herd 7 and all the large herds had antibiotic protocols to treat clinical mastitis and dairy herds 8, 12 and 13 employed a mastitis specialist.

2.5. Study design and disease recording

A total of 5375 Holstein dairy cows (1316 PP and 4059 MP) that calved between 1 March 2016 and 1 March 2017 were evaluated. Data for each individual cow included: parity (PP or MP), milk yield (at the first three monthly herd tests), calving date and description (calf sex, stillbirth, single or twin), calving season (autumn-winter: March to August; spring-summer: September to February), disease events in the first 90 DIM and also culling and reproductive parameters until 300 DIM. The date of the first service and the date of conception were recorded, as well as the date of culling. Culling in this study was defined as any cow that died or those that were sold for slaughter. We considered involuntary culling as the removal of animals from the herd, implying that if the cause or event had been avoided, the cow would have had sufficient merit to remain in the herd (Stevenson and Lean, 1998). Herd managers were asked to register the cause of death or the reason of culling from the herd. Herd managers were instructed to record only disease events (described below) that required treatment and they received a protocol to standardize disease definition prior to the start of the study. Stillbirth was defined as a calf born dead or a calf that died within 24 h of birth (Juozaitiene et al., 2017). Retained placenta and metritis (RP-metritis) were treated as a single uterine disease (Carvalho et al., 2019). The definition was failure to expel the placenta within 24 h after parturition (LeBlanc, 2008) and/or a fetid watery red-brown uterine discharge, associated with signs of systemic illness (decreased milk yield, dullness or other signs of toxemia) and fever >39.5 °C (Sheldon et al., 2006). Milk fever was defined as a cow with clinical signs of milk fever, such as muscular weakness (Berge and Vertenten, 2014) or recumbency, with a positive response to calcium treatment (Sepúlveda Varas et al., 2015). Recumbent cow disorder was defined as a cow that was unable to stand up (Correa et al., 1993) with lack of response to calcium treatment. The definition of clinical mastitis (CM) included all cows with abnormal milk or inflammation in one or more quarters (McDougall et al., 2008) detected and treated by the milkers. Lameness was defined as cows treated for foot problems (Bargo et al., 2009). Other diseases included cows treated for indigestion (defined as change in fecal consistency (Berge and Vertenten, 2014), decreased appetite and absence of rumination), bovine leukosis diagnosed by the veterinarian and miscellaneous disease (bovine actinomycosis, abscess, fever).

2.6. Statistical analysis

Statistical analyses were performed with SAS University (version 9.4, SAS Institute Inc., Cary, NC), considering the cow as the unit of interest. Disease cumulative incidence was summarized through descriptive statistics according to parity (PP vs MP) and herd size (SH vs LH) using FREQ and MEANS procedures. Before application of multivariable models, a stratified analysis was performed. All the disease events were coded as 0, 1 (yes, no) dichotomous variables. To evaluate the association between stillbirth and twins, a multivariable logistic regression (MLR) using GLIMMIX procedures were used considering parity and herd size as fixed effects and herd as random effect. To evaluate the risk of peripartum diseases (RP-metritis, mastitis, lameness) according to parity (PP and MP) and herd size (SH and LH), data were analyzed by MLR using GLIMMIX procedures of SAS. Dairy herd was included as a random effect. The model for RP-metritis also included stillbirth and twin birth. To test the effect of parity (PP vs. MP) on CM incidence up to 14 DIM, GLIMMIX procedures were performed considering herd size and parity as fixed effects and herd as random effect. The analysis was made considering variation among cows inside a herd. Culling and fertility outcomes (first service and pregnancy) were analyzed using Cox's proportional hazard analyses, using PHREG procedures of SAS. A manual backward selection procedure was used to build the final models. Based on Akaike's information criterion, the best fitting model was selected. Assumptions on the proportional hazard risk were verified as suggested by Dohoo et al. (2003). Additionally, a frailty model was adjusted considering herd as a random effect in the 3 models. Two way interactions were also evaluated in the models. Statistical significance was set at $P \leq 0.05$. The 3 final models included the fixed effects of parity and herd size (as forced variables), diseases (RP-metritis, mastitis and lameness) as categorical variables and milk production as a continuous variable (using the milk yield mean of the first three monthly herd tests). For the fertility models (first service and pregnancy) dairy herd 9 was excluded from the models, because it was the only herd with a split calving season.

3. Results

3.1. Disease incidence

From a total of 5375 cows, 24.5% were PP cows (n=1316). Overall, 36.5% (n=1959) of the cows monitored had at least one clinical disease during the first 90 DIM. Disease incidence and calving characteristics according to parity and herd size are shown in Tables 1 and 2.

Clinical mastitis was the most frequent disease, with an overall incidence of 27.6% (n=1483) during the first 90 DIM. After performing MLR, CM was affected by parity, with higher odds in MP than in PP cows (OR=1.8; 95% confidence interval (CI)=1.6–2.2), and by herd size, with higher odds in large herds (OR=2.5; 95 % CI = 1.3–5.1) (Table 3). The median of days to the first CM case was 14 (4–43, Q1-Q3) DIM. However, the proportion of cows with CM within these 14 DIM was different according to parity: in PP cows, from the total cases of CM (n=226) 61% (n=137) occurred during the first 14 DIM, although in MP cows, from the total cases (n=1256) only 49% (n=612) occurred during the first 14 DIM. In the MLR the odds of CM in the first 14 DIM was 1.3 (95% CI=1.1–1.6) times higher in PP than MP cows.

The overall cumulative incidence of RP-metritis was 4.4% (n=235), while the mean and median time to RP-metritis diagnosis was 7 (±12, SD) and 3 (2–6, Q1-Q3) DIM respectively. After performing MLR, herd size was not significant (Table 3). However parity was significant. The odds of RP-metritis increased in MP cows (OR=1.4; 95% CI=1.0–2.0), after adjustment by stillbirth and twins. The odds of RP-metritis were 3 (95% CI=1.5–5.0) times higher for cows with twin birth, and were 4 (95% CI=2.9–6.5) times higher in cows with stillbirth (Table 3).

Lameness incidence in the first 90 DIM was 5.0% (n=269) and was not affected by parity, but was affected by herd size, being greater in large herds (OR=2.4; 95% CI=1.6–3.9) in the MLR model (Table 3). Mean time from calving to diagnosis was 36 DIM (±27.1, SD). Diseases such as milk fever, recumbent cow syndrome, bovine leukosis, indigestion and others had very low incidence, less than 1%, reason why there were not analyzed due to the lack of statistical power. Overall, twin birth and stillbirth incidence were 2.2% (n=118) and 4.9% (n=264) respectively. There was no effect of herd size, but parity affected both (Table 1 and 2). The odds of being a dead calf were higher in twin births than in single births (OR=6.8; 95% CI=4.3–10.8).

3.2. Reproduction

Overall, 78.7% (n=3456) of the cows in the study were inseminated. This percentage was affected by parity (PP=83.9% (n=774) vs. MP = 77.4% (n=2682), $P< 0.01$) and herd size (SH = 86.7 % (n = 814) vs. LH = 76.6 % (n = 2642), $P < 0.01$). Mean and median calving to first AI interval was 84 (± 44, SD) and 76 (54–99, Q1-Q3) days respectively and 76.2 % (n = 2634) of the cows received their first AI within the first 100 DIM. In the final model, considering 300 DIM, all the variables considered in the model were significant for time to first AI, with the exception of herd size (Table 4). The insemination hazard rate (HR) was 12 % lower for MP cows respect of PP cows (HR = 0.88, 95 % CI =

Table 1
Calving characteristics and disease cumulative incidence over the first 90 DIM of dairy cows in 13 grazing dairy herds in Uruguay, according to parity [Primiparous cows (PP), n=1316, Multiparous cows (MP), n=4059].

Variable	Overall n (%)	PP n (%)	MP n (%)
Twins	118 (2.2)	9 (0.7)	109 (2.7)
Stillbirth	264 (4.9)	91 (6.9)	173 (4.3)
RP-MET[a]	235 (4.4)	50 (3.8)	185 (4.6)
MAST[b]	1483 (27.6)	226 (17.2)	1257 (30.9)
LAME[c]	269 (5.0)	76 (5.8)	193 (4.7)
Others[d]	163 (3.0)	10 (0.76)	153 (3.7)
Sick cows[e]	1959 (36.5)	337 (25.6)	1622 (39.9)

[a] Retained placenta-metritis.
[b] Clinical Mastitis.
[c] Lameness.
[d] Others: downer cow, hypocalcemia, leukosis, indigestion among others.
[e] Sick cows: Cows with any of the preceding diseases.

Table 2
Calving characteristics and mean, minimun and maximun disease cumulative incidence over the first 90 DIM of dairy cows in 13 grazing dairy herds in Uruguay according to herd size [Cows in small herds (SH), n=939, cows in large herds (LH), n=4436].

	SH (n=939)			LH (n=4436)		
	Mean	Min	Max	Mean	Min	Max
Twins	2.0	0.0	7.0	2.2	1.0	3.8
Stillbirth	5.4	0.0	11.0	4.8	3.6	5.6
RP-MET[a]	6.6	1.0	13.0	3.9	0.3	7.5
MAST[b]	19.1	5.8	37.0	29.4	15.8	43.8
LAME[c]	2.3	0.0	5.6	5.6	3.5	8.4
Others[d]	2.88	0.6	5.1	3.1	0.7	8.8
Sick cows[e]	26.6	10.4	45.7	38.5	25.3	48.7

[a] Retained placenta-metritis.
[b] Clinical Mastitis.
[c] Lameness.
[d] Others: downer cow, hypocalcemia, leukosis, indigestion among others.
[e] Sick cows: Cows that had any of the diseases below.

Table 3
Multivariable logistic regression model estimates for retained placenta-metritis, mastitis and lameness in 13 grazing dairy herds in Uruguay.

RP-metritis	Variable	Value	Estimate	SE	OR	95 %CI	t value	Pr > |t|
	Intercept		−3.49	0.45			−7.79	<0.01
	Parity	MP vs PP	0.36	0.17	1.44	1.02−2.02	2.08	<0.05
	Herd size	LH vs SH	−0.51	0.60	0.59	0.18−1.95	−0.86	NS
	Stillbirth	Dead vs live	1.47	0.20	4.36	2.92−6.51	7.20	<0.01
	Twins	Twin vs single	1.02	0.30	2.77	1.52−5.05	3.33	<0.01
Mastitis	**Variable**	**Value**	**Estimate**	**SE**	**OR**	**95 %CI**	**t value**	**Pr > |t|**
	Intercept		−2.17	0.26			−8.30	<0.01
	Parity	MP vs PP	0.61	0.08	1.84	1.56−2.18	7.13	<0.01
	Herd size	LH vs SH	0.93	0.35	2.54	1.26−5.09	2.62	<0.01
Lameness	**Variable**	**Value**	**Estimate**	**SE**	**OR**	**95 %CI**	**t value**	**Pr > |t|**
	Intercept		−3.58	0.23			−15.03	<0.01
	Parity	MP vs PP	−0.20	0.13	0.82	0.62−1.07	−1.45	NS
	Herd size	LH vs SH	0.89	0.22	2.45	1.58−3.82	3.98	<0.01

OR= Odd Ratio
CI= Confidence interval
MP= Multiparous cows
PP= Primiparous cows.
LH= large herds
SH= Small herds
NS= No significant

Table 4
Final Cox proportional hazards model factors associated with time to first service in 13 grazing dairy herds in Uruguay.

Variable	Class	Estimate	SE	HR	95 %CI	Pr > ChiSq
Parity	MP vs PP	−0.12	0.05	0.88	0.79−0.98	<0.05
Herd size	LH vs SH	−0.18	0.12	0.83	0.67−1.05	NS
RP-MET[a]	Present vs NP[d]	−0.36	0.10	0.70	0.57−0.85	<0.01
MAST[b]	Present vs NP[d]	−0.48	0.19	0.61	.	<0.05
LAME[c]	Present vs NP[d]	−0.63	0.11	0.53	.	<0.01
Twins	Twin vs single	−0.26	0.12	0.76	0.61−0.96	<0.05
Milk yield		0.015	0.004	1.012	.	<0.01

MP = Multiparous cows
PP = Primiparous cows.
LH = large herds
SH = Small herds
HR= Hazard ratio
CI = Confidence interval
[a] Retained placenta-metritis.
[b] Clinical mastitis.
[c] Lameness.
[d] NP = Not present.

0.79−0.98). Cows with CM, lameness, RP-metritis and twin births showed 39 %, 47 %, 31 % and 24 % lower insemination HR, respectively (Table 4). Milk yield showed slightly but significant effect with a 1.2 % increase in the HR of the first service for every litre of increase in production. This final model also retained the interaction of mastitis and lameness, which unexpectedly showed a relative increased in the insemination HR.

The overall pregnancy risk was 66.6% (n=2922) at the end of the study (300 DIM). The total proportion of pregnant cows was affected by parity (PP=75.8% (n=700) vs. MP=64.1% (n=2222), P<0.01). Proportion of pregnant cows was also affected by herd size [SH=74.2% (n=697) vs. LH=64.5% (n=2225), P< 0.01]. Mean and median calving to conception interval was 116.5 (± 57.5, SD) and 103 (75–148, Q1-Q3) DIM. Moreover, 48.2% (n=2922) of the cows got pregnant within the first 100 DIM. In the Cox regression model, considering 300 DIM, all the variables were significant, with the exception of herd size (Table 5). The pregnancy HR for MP cows was 20% lower respect of PP cows (HR=0.80, 95% CI=0.73−0.88). Cows with CM, RP-metritis, lameness and stillbirth were 12% (HR=0.88, 95% CI=0.81−0.96), 36% (HR=0.64, 95% CI=0.52−0.79), 38% (HR=0.62, 95% CI=0.51−0.75) and 30% (HR=0.70, 95% CI=0.58−0.85) lower pregnancy HR, respectively.

3.3. *Culling*

From the 5375 cows, 20.6% (n=1108) were culled before the end of the study (300 DIM). The median of the days to culling was 107 (42–184 Q1-Q3) DIM. From the total culling, 44% (n=487) occurred in the first 90 DIM. Culling was affected by parity (MP=22.2%, n=903 vs. PP=15.6%, P< 0.01) and herd size (LH=22.3% n=988 vs. SH=12.8%

Table 5
Final Cox proportional hazard model factors associated with time to pregnancy in 13 grazing dairy herds in Uruguay.

Variable	Class	Estimate	SE	HR	95 %CI	Pr > ChiSq
Parity	MP vs PP	−0.22	0.04	0.80	0.73−0.88	<0.01
Herd size	LH vs SH	0.02	0.10	1.02	0.84−1.24	NS
MAST[a]	Present vs NP[d]	−0.12	0.04	0.88	0.81−0.96	<0.05
RP-MET[b]	Present vs NP[d]	−0.43	0.10	0.64	0.52−0.80	<0.01
LAME[c]	Present vs NP[d]	−0.48	0.09	0.62	0.51−0.75	<0.01
Stillbirth	Present vs NP[d]	−0.35	0.09	0.70	0.58−0.85	<0.01

MP = Multiparous cows
PP = Primiparous cows.
LH = large herds
SH = Small herds
HR= Hazard ratio
CI = Confidence interval.
NS = No significant
[a] Clinical mastitis.
[b] Retained placenta-metritis.
[c] Lameness.
[d] NP = not present.

n=120, P< 0.01). Final model results showed that parity was associated with hazard of culling, as MP cows had increased hazard of culling (HR=2.9, 95% CI=2.3–3.8) compared with PP cows (Table 6). The culling HR was 2.3 (95% CI=1.98−2.76) times higher for cows with CM and 1.6 (95% CI=1.2–2.2) times higher for lame cows.

4. Discussion

The disease incidence in the first 90 DIM found in this study (36.5%) is similar to the incidence reported in other studies performed in grazing systems (Stevenson, 2000; Sepúlveda Varas et al., 2015). However, it is difficult to compare disease incidences between studies, because diagnostic criteria and record management may differ (Stevenson, 2000). In our study, MP cows had a higher proportion of affected animals in comparison to PP cows, and this was also reported in Argentina by Bargo et al. (2009). Nevertheless, in their study the percentage of sick MP cows was higher than in ours (67% vs. 40.0%), and although they had a similar disease definition and register of events than ours, they studied 37 dairy farms being a three year-long study. According to herd size, most studies report disease prevalence instead of disease cumulative incidence in the first 90 DIM as we do, therefore in order to compare with others studies this fact must be taken into account. Also, study designs in the existing literature differ considerably and the definition of large and small herd sizes, are country specific. Cows in small herds had less clinical disease events, as reported by Hill et al. (2009), who also found that the likelihood of disease increased in large herds. However, Beggs et al. (2019) found no difference in disease prevalence among different herd sizes in grazing dairy systems, and neither did Gieseke et al. (2018) in freestall housing systems.

Twin birth (2.2%) and stillbirth (4.9%) incidence was similar to other studies in grazing systems [McDougall, 2001 (1.5%; 9.4%); Mee et al., 2008 (2.7%; 4.3%); Hayes et al., 2012 (3.3%; 8.2%)]. The higher incidence of twins in MP cows is in agreement with Silva del Río et al. (2007). This might occur because the multiple ovulation rate increases in older cows (Macmillan et al., 2018). Moreover, twin birth affected stillbirth, in agreement with others (Silva del Río et al., 2007; Berry et al., 2007), which is mainly due to a shorter gestation period (Nielen et al., 1989). It should be noted that twin birth is also a risk factor for dystocia and therefore for calf mortality (Berry et al., 2007). The incidence of twins was lower in primiparous cows, although stillbirth was greater (6.9% vs. 4.3%). Similar, Mee et al. (2008) reported 7.7% and 3.5% of stillbirth in PP and MP, respectively, mainly explained by higher calving assistance and dystocia in PP cows (Mee et al., 2008; Bleul, 2011), which is one of the most important risk factors for stillbirth (Meyer et al., 2000). Herd size had no effect on these variables, in agreement with Mee et al. (2008). However, Silva del Río et al. (2007) reported an increase in calf mortality as herd size increased; they postulated that individual cows may be less intensively managed during calving in larger herds and/or calf mortality may be more accurately reported than in smaller herds.

Table 6
Final Cox proportional hazard model factors associated with time to culling in 13 grazing dairy herds in Uruguay.

Variable	Class	Estimate	SE	HR	95 %CI	Pr > ChiSq
Parity	MP vs PP	1.08	0.13	2.94	2.26−3.82	<0.01
Herd size	LH vs SH	0.36	0.24	1.43	0.89−2.32	NS
MAST[a]	Present vs NP[c]	0.85	0.08	2.34	1.98−2.76	<0.01
LAME[b]	Present vs NP[c]	0.49	0.15	1.64	1.23−2.21	<0.01
Milk yield		−0.07	0.008	0.93	0.91−0.94	<0.01

MP = Multiparous cows.
PP = Primiparous cows.
LH = large herds.
SH = Small herds.
HR= Hazard ratio.
CI = Confidence interval.
NS = No significant.
[a] Clinical mastitis.
[b] Lameness.
[c] Not present.

In the present study, the overall incidence of RP-metritis (4.4%) was lower than the range reported for RP and metritis mentioned in grazing systems that varies between 5.3% and 41.1% (Hayes et al., 2012; Sepúlveda Varas et al., 2015; Sepúlveda Varas and Wittwer Menge, 2017; Carvalho et al., 2019). We used a single disease definition for RP-metritis, as did Carvalho et al. (2019), because the farms in our study did not make a distinction between RP and puerperal metritis: both were treated with antibiotics. In most of the aforementioned studies, the researcher or veterinarian of the dairy herd diagnosed the disease following a postpartum monitoring protocol. We relied on the farm worker to make the diagnosis, and therefore the incidence in our study may have been underestimated. The MP cows had a higher odds of RP-metritis, in agreement with others (Kaneene and Miller, 1994; Daros et al., 2017), possibly associated with a higher incidence of RP and a higher incidence of subclinical hypocalcemia and subclinical ketosis (Curtis et al., 1983; Martínez et al., 2012; Berge and Vertenten, 2014) considering that severe negative energy balance impairs immune function (LeBlanc, 2010). However, some authors report a higher risk of metritis in PP cows (Markusfeld, 1984; Toni et al., 2015), associated with a higher risk of dystocia (Kaneene and Miller, 1994). We found that stillbirth and twin birth are associated with RP-metritis, which is in agreement with others (Muller and Owens, 1974; Markusfeld, 1984; Oltenacu et al., 1990; Chassagne et al., 1999; McDougall, 2001). This is thought to be associated with increased calving assistance and dystocia (Meyer et al., 2000; Berry et al., 2007; Bleul, 2011) which may increase uterus contamination because of the human intervention (Dubuc et al., 2010). Herd size was not associated with RP-metritis in agreement with Bruun et al. (2002). However, some researchers found more cows with RP-metritis in larger herds, presumably associated with different management practices such as better detection and disease recording (Fourichon et al., 2001).

Overall incidence of CM in the first 90 DIM in the present study (27.6%) was higher than the reported in another study in a grazing system, that studied CM incidence during a full lactation (Petrovski et al., 2009, 14.8%). Clinical mastitis is a multifactorial disease, but the high incidence in our study could be partially attributed to the rainy weather in April 2016, a month in which it rained 360 mm in the area in which the farms are situated, while the historical average is 90 mm (Inumet, 2020). Many farm tracks collapsed and the paddocks for springing and lactating cows on most farms became very muddy and wet. It has been reported that poor udder hygiene is a risk factor for mastitis (Ruegg, 2009). Unfortunately in the present study the type of mastitis (environmental or contagious mastitis) was not diagnosed. In our study, MP cows had a higher odds for CM than PP cows, in accordance with other studies (Petrovski et al., 2009; Richardet et al., 2016). This may be explained because older cows have higher milk yields (Ingvartsen et al., 2003), which is associated with higher odds of clinical mastitis (Oltenacu and Ekesbo, 1994) and subclinical hypocalcemia, which in turn reduces the contraction of the teat sphincter muscle and affects immune function (Kimura et al., 2006; Goff, 2014). Indeed, it was reported that older cows might be related to the decrease in the integrity of the streak canal (Cousins et al., 1980) and teat sphincter patency as udder defence mechanisms may deteriorate with age (Dingwell et al., 2004). Also, MP cows, because of their previous lactations, increase their risk of CM in the subsequent lactation (Pantoja et al., 2009; Pinedo et al., 2012). Finally, the odds of ketosis is higher in MP cows (Berge and Vertenten, 2014) which is associated to higher odds of mastitis (LeBlanc, 2010; Berge and Vertenten, 2014) related to the impairment of udder defence mechanisms during hyperketonemia (Suriyasathaporn et al., 2000). However, in the first two weeks postpartum, mastitis as a percentage of total cases was higher in PP than MP cows, in agreement with others (Barkema et al., 1998; Olde Riekerink et al., 2008). Risk factors for PP are different than for MP cows; the PP cows are still growing and they are going through the process of adaptation to lactation and milking management (Parker et al., 2007). One risk factor for CM reported in PP cows is mixing them with MP cows after calving (Parker et al., 2007). In the present study, only herd 11 managed a heifer mob, (a separate group from adult cows).

The odds for CM were greater in large herds, which may be associated with management. For instance, large herds concentrate calving in autumn, a rainy season. The high number of animals being in their highest risk period for diseases could increase CM incidence. This could be due to greater exposure to environmental pathogens (high stocking density in calving paddocks in which hygiene is difficult to manage and feeding areas that are difficult to keep clean) and an increase in the number of cows milked per person as reported previously (Parker et al., 2007). On the other hand, Hill et al. (2009) reported decreased disease prevalence as herd size increased, and explained that management in large herds may be better than in small herds and thus, contribute to a lower disease prevalence.

Overall incidence of lameness in our study was 5%, lower than previous reports in New Zealand herds (10%, Chesterton, 2006). However, to make a correct diagnosis, an appropriate infrastructure is required, which was not present in our study; thus, this incidence could be underestimated. No significant difference was found according to parity, although in a study carried out in an Uruguayan grazing dairy herd during 4 years, it was found that lameness was more frequent in PP than MP cows (24% vs. 15.9%) (Ramos and Freire, 2006). The authors attribute this to the fact that excessive wear of the sole and bruising are more common in younger cows. Nevertheless, in other studies, MP cows were more likely to be lame (Rutherford et al., 2009), associated with heavier body weight (Wells et al., 1993). We found a greater lameness odds in large herds, Flor and Tadich, 2008 reported higher prevalence of lame cows in larger herds, probably due to longer walking distances. In the present study cows in the SH walked in average (SD) 3.2 (± 1.3) km per day while cows in LH walked in average (SD) 5.9 (± 1.8) km per day.

In the final model, PP cows had a higher first insemination HR, this result was not expected. Indeed, as reported, PP cows have delayed interval to first AI (Butler and Smith, 1989; Meikle et al., 2004) associated to longer anestrous duration because of the NEB, that in heifers could be due to lower DMI, ascendant lactation curve and/or growth requirements (Meikle et al., 2004). Pregnancy HR was also affected by parity, with a higher pregnancy HR for PP cows. This could be associated with less metabolic stress in this category due to lower milk yield in the early postpartum period as reported by Galvão et al. (2010). Also, MP cows have a larger uterine size, being a reason for negative effect on fertility in comparison to PP cows (Baez et al., 2016).

Retained placenta-metritis, CM and lameness had a negative effect on first AI and pregnancy HR, in agreement with others (Santos et al., 2004; Hayes et al., 2012; Ribeiro et al., 2013; Toni et al., 2015; Pinedo et al., 2016). Indeed, it has been reported that disease negatively affects fertility, delaying cyclicality after calving and compromising embryo development because of inflammatory mediators (Cullor, 1990; Sheldon et al., 2002; Soto et al., 2003). Disease could also be associated with lower feed intake, exacerbating NEB and loss of body condition, which delays the resumption of ovarian cyclicality and increases the risk for low conception rates (Butler, 2000). Stillbirth affected pregnancy HR and twin birth affected first AI HR, both of which are closely associated with RP-metritis (a risk factor in the present study) (Grohn et al., 1990; Giuliodori et al., 2013). Moreover, milk production affected time to first AI, however Toni et al. (2015) did not found an association between milk yield and first AI.

The greater HR for culling in MP cows in our study is in agreement with others (Rajala-Schultz and Grohn, 1999; De Vries et al., 2010; Dubuc et al., 2011), and could be associated to the fact that to achieve economic amortization of the heifers cost they must stay at the herd more than one lactation (Seegers et al., 1998; Boulton et al., 2017). Also it could be associated to the higher disease incidence in this category (Shahid et al., 2015) as was shown in Table 1. Moreover, the involuntary culling HR for cows with CM and lameness was higher than for healthy cows, as was also reported by others (Grohn et al., 1998; Santos et al., 2004; Booth et al., 2004; del P Schneider et al., 2007; Bar et al., 2008). A sick cow causes greater economic losses related to antibiotic treatment, non-saleable milk, veterinary costs and lower milk production (Galligan, 2006; Rollin et al., 2015). Higher yielding cows had less culling HR, as reported previously (Grohn et al., 1998), possibly because disease depresses milk yield.

Overall, health problems had a negative impact on indicators of dairy herd fertility and culling; also, disease incidence in early lactation was high and showed a wide variation among herds, revealing the importance of preventive herd health program which could improve cow reproductive performance and reduce the hazard of culling.

5. Conclusions

According to the study finding, we conclude that in these grazing dairy farms in Uruguay, mastitis was the disease of greater incidence. Multiparous cows had more mastitis and retained placenta-metritis than primiparous cows. Clinical mastitis and lameness incidence was higher in large than in small herds. Moreover, disease has a negative impact on reproductive performance and increases involuntary culling.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

We thank dairy farmers and their workers for participating in this project. We thank Mette Bowman for providing language help. This research was supported by the National Research and Innovation Agency (ANII, Uruguay), [Grant No. POS_NAC_2016_1_129928].

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.prevetmed.2021.105359.

References

Armengol, R., Fraile, L., 2018. Descriptive study for culling and mortality in five high-producing Spanish dairy cattle farms (2006-2016). Acta Vet. Scand. 60, 45.
Baez, G.M., Barletta, R.V., Guenther, J.N., Gaska, J.M., Wiltbank, M.C., 2016. Effect of uterine size on fertility of lactating dairy cows. Theriogenology 85, 1357–1366.
Bar, D., Tauer, L.W., Bennett, G., González, R.N., Hertl, J.A., Schulte, H.F., Schukken, Y. H., Welcome, F.L., Gröhn, Y.T., 2008. Use of a dynamic programming model to estimate the value of clinical mastitis treatment and prevention options utilized by dairy producers. Agric. Syst. 99, 6–12.
Bargo, F., Busso, F., Corbellini, C., Grigera, J., Lucas, V., Podetti, V., Vidaurreta, Tuñon Gy, 2009. Organization and analysis of a system of registers of peripartum diseases in dairy cows: its incidence and economic impact on companies. Final report 1, 1–44. http://www.pmpl-laserenisima.com.ar:8090/Images/comunicados/noticias/Reporte%20final%20Claves.pdf.
Barkema, H.W., Schukken, Y.H., Lam, T.J.G.M., Beiboer, M.L., Benedictus, G., Brand, A., 1998. Management practices associated with low, medium, and high somatic cell counts in bulk milk. J. Dairy Sci. 81, 1917–1927.
Beggs, D.S., Fisher, A.D., Jongman, E.C., Hemsworth, P.H., 2015. A survey of Australian dairy farmers to investigate animal welfare risks associated with increasing scale of production. J. Dairy Sci. 98, 5330–5338.
Beggs, D.S., Jongman, E.C., Hemsworth, P.H., Fisher, A.D., 2019. The effects of herd size on the welfare of dairy cows in a pasture-based system using animal- and resource-based indicators. J. Dairy Sci. 102, 3406–3420.
Berge, A.C., Vertenten, G., 2014. A field study to determine the prevalence, dairy herd management systems, and fresh cow clinical conditions associated with ketosis in western European dairy herds. J. Dairy Sci. 97, 2145–2154.

Berry, D.P., Lee, J.M., Macdonald, K.A., Roche, J.R., 2007. Body condition score and body weight effects on Dystocia and stillbirths and consequent effects on postcalving performance. J. Dairy Sci. 90, 4201–4211.
Bleul, U., 2011. Risk factors and rates of perinatal and postnatal mortality in cattle in Switzerland. Livest. Sci. 135, 257–264.
Booth, C.J., Warnick, L.D., Grohn, Y.T., Maizon, D.O., Guard, C.L., Janssen, D., 2004. Effect of lameness on culling in dairy cows. J. Dairy Sci. 87, 4115–4122.
Boulton, A.C., Rushton, J., Wathes, D.C., 2017. An empirical analysis of the cost of rearing dairy heifers from birth to first calving and the time taken to repay these costs. Animal 11 (8), 1372–1380.
Bruun, J., Ersbølla, A.K., Alban, L., 2002. Risk factors for metritis in Danish dairy cows. Prev. Vet. Med. 54, 179–190.
Butler, W.R., 2000. Nutritional interactions with reproductive performance in dairy cattle. Anim. Reprod. Sci. 60–61, 449–457.
Butler, W.R., Smith, R.D., 1989. Interrelationships between energy balance and postpartum reproductive function in dairy cattle. J. Dairy Sci. 72, 767–783.
Carvalho, M.R., Peñagaricano, F., Santos, J.E.P., DeVries, T.J., McBride, B.W., Ribeiro, E. S., 2019. Long-term effects of postpartum clinical disease on milk production, reproduction and culling of dairy cows. J. Dairy Sci. 102, 11701–11717.
Chassagne, M., Barnouin, J., Chacornac, J.P., 1999. Risk factors for stillbirth in Holstein heifers under field conditions in France: a prospective survey. Theriogenology 51, 1477-1466.
Chesterton, N., 2006. Lameness under grazing conditions. 14th International Symposium and 6th Conference on Lameness in Ruminants - Colonia-Uruguay 8-11 Nov. 2006.
Compton, C.W.R., Heuer, C., Parker, K., McDougall, S., 2007. Risk factors for peripartum mastitis in pasture-grazed dairy heifers. J. Dairy Sci. 90, 4171–4180.
Correa, M.T., Erb, H., Scarlett, J., 1993. Path analysis for seven postpartum disorders of Holstein cows. J. Dairy Sci. 76, 1305–1312.
Cousins, C.L., Higgs, T.M., Jackson, E.R., Neave, F.K., Dodd, F.H., 1980. Susceptibility of the bovine udder to bacterial infection in the dry period. J. Dairy Res. 47, 11–18.
Cullor, J.S., 1990. Mastitis and its influence upon reproductive performance in dairy cattle. In: Proceedings of the International Symposium on Bovine Mastitis. Indianapolis, IN, pp. 175–180.
Curtis, C.R., Erb, H.N., Sniffen, C.J., Smith, R.D., Powers, P.A., Smith, M.C., White, M.E., Hillman, R.B., Pearson, E.J., 1983. Association of parturient hypocalcemia with eight periparturient disorders in Holstein cows. J. Am. Vet. Med. Assoc. 183, 559.
Daros, R.R., Hötzel, M.J., Bran, J.A., LeBlanc, S.J., von Keyserlingk, M.A.G., 2017. Prevalence and risk factors for transition period diseases in grazing dairy cows in Brazil. Prev. Vet. Med. 145, 16–22.
De Vries, A., Olson, J.D., Pinedo, P.J., 2010. Reproductive risk factors for culling and productive life in large dairy herds in the eastern United States between 2001 and 2006. J. Dairy Sci. 93, 613–623.
del P Schneider, M., Strandberg, E., Emanuelson, U., Grandinson, K., Roth, A., 2007. The effect of veterinary-treated clinical mastitis and pregnancy status on culling in Swedish dairy cows. Prev. Vet. Med. 80, 179–192.
Detilleux, J.C., Kehrli, M.E., Stabel, J.R., Freeman, A.E., Kelley, D.H., 1995. Study of immunological dysfunction in periparturient Holstein cattle selected for high and average milk production. Veterinay Immunology and Immunopathology 44, 251–267.
Dingwell, R.T., Leslie, K.E., Schukken, Y.H., Sargeant, J.M., Timms, L.L., Duffield, T.F., Keefe, G.P., Kelton, D.F., Lissemore, K.D., Conklin, J., 2004. Association of cow and quarter-level factors at drying-off with new intramammary infections during the dry period. Prev. Vet. Med. 63, 75–89.
Dohoo, I.R., Martin, W., Stryhn, H., 2003. Veterinary Epidemiologic Research. Atlantic Veterinary College Inc., University of Prince Edward Island, Prince Edward Island Canada.
Drackley, J.K., 1999. Biology of Dairy Cows During the Transition Period: the Final Frontier? J. Dairy Sci. 82, 2259–2273.
Dubuc, J., Duffield, T.F., Leslie, K.E., Walton, J.S., LeBlanc, S.J., 2010. Risk factors for postpartum uterine diseases in dairy cows. J. Dairy Sci. 93, 5764–5771.
Dubuc, J., Duffield, T.F., Leslie, K.E., Walton, J.S., LeBlanc, S.J., 2011. Effects of postpartum uterine diseases on milk production and culling in dairy cows. J. Dairy Sci. 94, 1339–1346.
Eicher, S.D., Schutz, M., Kearney, F., Willard, S., Bowers, S., Gandy, S., Graves, K., 2007. Prepartum milking effects on parlour behaviour, endocrine and immune responses in Holstein heifers. J. Dairy Res. 74, 417–424.
Flor, E., Tadich, N., 2008. Lameness in cows from large and small dairy herds in southern Chile. Arch. Med. Vet. 40, 125–134.
Fourichon, C., Beaudeau, F., Bareille, N., Seegers, H., 2001. Incidence of health disorders in dairy farming systems in western France. Livest. Prod. Sci. 68, 157–170.
Galligan, D., 2006. Economic Assessment of animal health performance. Veterinary Clinics Food Animal Practice 22, 207–227.
Galvão, K.N., Flaminio, M.J.B.F., Brittin, S.B., Sper, R., Fraga, M., Caixeta, L., Ricci, A., Guard, C.L., Butler, W.R., Gilbert, R.O., 2010. Association between uterine disease and indicators of neutrophil and systemic energy status in lactating Holstein cows. J. Dairy Sci. 93, 2926–2937.
Gieseke, D., Lambertz, C., Gauly, M., 2018. Relationship between herd size and measures of animal welfare on dairy cattle farms with freestall housing in Germany. J. Dairy Sci. 101, 7397–7411.
Giuliodori, M.J., Magnasco, R.P., Becu-Villalobos, D., Lacau-Mengido, I.M., Risco, C.A., De la Sota, R.L., 2013. Metritis in dairy cows: risk factors and reproductive performance. J. Dairy Sci. 96, 3621–3631.
Goff, J.P., 2014. Calcium and magnesium disorders. Veterinary Clin. Food Animal Pract. 30, 359–381.
Goff, J.P., Horst, R.L., 1997. Physiology and management: physiological changes at Parturition and their relationship to metabolic disorders. J. Dairy Sci. 80, 1260–1268.
Goldberg, J.J., Wildman, E.E., Pankey, J.W., Kunkel, J.R., Howard, D.B., Murphy, B.M., 1992. The influence of intensively managed rotational grazing, traditional continuous grazing, and confinement housing on bulk tank milk quality and udder health. J. Dairy Sci. 75, 96–104.
Grohn, Y.T., Erb, H.N., McCulloch, C.E., Saloniemi, H.S., 1990. Epidemiology of reproductive disorders in dairy cattle: associations among host characteristics, disease and production. Prev. Vet. Med. 8, 25–39.
Grohn, Y.T., Eicker, S.W., Ducrocq, V., Hertl, J.A., 1998. Effect of diseases on the culling of holstein dairy cows in New York State. J. Dairy Sci. 81, 966–978.
Hayes, E.P.B., Christley, R.M., Dobson, H., 2012. Effects of periparturient events on subsequent culling and fertility in eight UK dairy herds. Vet. Rec. 170, 540.
Hill, A.E., Green, A.L., Wagner, B.A., Dargatz, D.A., 2009. Relationship between herd size and annual prevalence of and primary antimicrobial treatments for common diseases on dairy operations in the United States. Prev. Vet. Med. 88, 264–277.
Ingvartsen, K.L., 2006. Feeding and management related diseases in the transition cow Physiological adaptations around calving and strategies to reduce feeding related diseases. Anim. Feed Sci. Technol. 126, 175–213.
Ingvartsen, K.L., Dewhurst, R.J., Friggens, N.C., 2003. On the relationship between lactational performance and health; is it yield or metabolic imbalance that causes production diseases in dairy cattle? A position paper. Livest. Prod. Sci. 73, 277–308.
INIA (January 2021). http://www.inia.uy/gras/Clima/Variables-clim%C3%A1ticas-INIA.
Inumet (October 2020) https://www.inumet.gub.uy/clima/estadisticas-climatologicas/graficas-estadisticas-pluviometricas.
Juozaitiene, V., Juozaitis, A., Kardisauskas, A., Zymantiene, J., Zilaitis, V., Antanaitis, R., Ruzauskas, M., 2017. Relationship between dystocia and the lactation number, stillbirth and mastitis prevalence in dairy cows. Acta Vet. Brno 86, 345–352.
Kaneene, J.B., Miller, R., 1994. Epidemiological study of metritis in Michigan dairy cattle. Vet. Res. 25 (2–3), 253–257.
Kerslake, J.I., Amer, P.R., O'Neill, P.L., Wong, S.L., Roche, J.R., Phyn, C.V.C.J., 2018. Economic costs of recorded reasons for cow mortality and culling in a pasture-based dairy industry. J. Dairy Sci. 101, 1795–1803.
Kimura, K., Reinhardt, T.A., Goff, J.P., 2006. Parturition and hypocalcemia blunts calcium signals in immune cells of dairy cattle. J. Dairy Sci. 89, 2588–2595.
LeBlanc, S., 2008. Postpartum uterine disease and dairy herd reproductive performance: a review. Vet. J. 176, 102–114.
LeBlanc, S., 2010. Monitoring metabolic health of dairy cattle in the transition period. J. Reprod. Dev. 56 (Suppl), S29–S35.
LeBlanc, S., Lissemore, K.D., Kelton, D.F., Duffield, T.F., Leslie, K.E., 2006. Major advances in disease prevention in dairy cattle. J. Dairy Sci. 89, 1267–1279.
Macmillan, K., Kastelic, J.P., Colazo, M.G., 2018. Update on multiple ovulations in dairy cattle. Animals 8, 62.
Markusfeld, O., 1984. Factors responsible for post parturient metritis in dairy cattle. Vet. Rec. 114, 539–542.
Martínez, N., Risco, C.A., Lima, F.S., Bisinotto, R.S., Greco, L.F., Ribeiro, E.S., Maunsell, F., Galvão, K., Santos, J.E.P., 2012. Evaluation of peripartal calcium status, energetic profile, and neutrophil function in dairy cows at low or high risk of developing uterine disease. J. Dairy Sci. 95, 7158–7172.
McConnel, C.S., 2010. Dissertation dairy cow mortality. Partial Fulfilment of the Requirements for the Degree of Doctor of Philosophy Colorado State University Fort Collins, Colorado.
McDougall, S., 2001. Effects of periparturient diseases and conditions on the reproductive performance of New Zealand dairy cows. N. Z. Vet. J. 49 (2), 60–67.
McDougall, S., 2003. Management factors associated with the incidence of clinical mastitis over the non-lactation period and bulk tank somatic cell count during the subsequent lactation. N. Z. Vet. J. 51 (2), 63–72.
McDougall, S., Parker, K.I., Weir, A.M., Compton, C.W.R., 2008. Effect of application of an external teat sealant and/or oral treatment with a monensin capsule pre-calving on the prevalence and incidence of subclinical and clinical mastitis in dairy heifers. N. Z. Vet. J. 56 (3), 120–129.
Mee, J.F., Berry, D.P., Cromie, A.R., 2008. Prevalence of, and risk factors associated with, perinatal calf mortality in pasture-based Holstein-Friesian cows. Animal 2 (4), 613–620.
Meikle, A., Kulcsar, M., Chilliard, Y., Febel, H., Delavaud, C., Cavestany, D., Chilibroste, P., 2004. Effects of parity and body condition at parturition on endocrine and reproductive parameters of the cow. Reproduction 127, 727–737.
Meyer, C.L., Berger, P.J., Koehler, K.J., 2000. Interactions among factors affecting stillbirths in holstein cattle in the United States. J. Dairy Sci. 83, 2657–2663.
Muller, L.D., Owens, M.J., 1974. Factors associated with the incidence of retained placentas. J. Dairy Sci. 57, 725–728.
Mulligan, F.J., Doherty, M.L., 2008. Production diseases of the transition cow. Vet. J. 176, 3–9.
Nielen, M., Schukken, Y.H., Scholl, D.T., Wilbrink, H.J., Brand, A., 1989. Twinning in dairy cattle: a study of risk factors and effects. Theriogenology 32 (5), 845–862.
Olde Riekerink, R.G.M., Barkema, H.W., Kelton, D.F., Scholl, D.T., 2008. Incidence rate of clinical mastitis on canadian dairy farms. J. Dairy Sci. 91, 1366–1377.
Oltenacu, P.A., Ekesbo, I., 1994. Epidemiological study of clinical mastitis in dairy cattle. Vet. Res. 25 (2–3), 208–212.
Oltenacu, P.A., Frick, A., Lindhé, B., 1990. Epidemiological study of several clinical diseases, reproductive performance and culling in primiparous Swedish cattle. Prev. Vet. Med. 9, 59–74.

Pantoja, J.C.F., Hulland, C., Ruegg, P.L., 2009. Somatic cell count status across the dry period as a risk factor for the development of clinical mastitis in the subsequent lactation. J. Dairy Sci. 92, 139–148.

Parker, K.I., Compton, C.W.R., Anniss, F.M., Weir, A.M., McDougall, S., 2007. Management of dairy heifers and its relationships with the incidence of clinical mastitis. N. Z. Vet. J. 55 (5), 208–216.

Petrovski, K.R., Heuer, C., Parkinson, T.J., Williamson, N.B., 2009. The incidence and aetiology of clinical bovine mastitis on 14 farms in Northland, New Zealand. N. Z. Vet. J. 57 (2), 109–115.

Pinedo, P.J., Fleming, C., Risco, C.A., 2012. Events occurring during the previous lactation, the dry period, and peripartum as risk factors for early lactation mastitis in cows receiving 2 different intramammary dry cow therapies. J. Dairy Sci. 95, 7015–7026.

Pinedo, P.J., Melendez, P., Paudyal, S., Krauss, R., Arias, F., Lopez, H., Luco, A., Vergara, C.F., 2016. Association between disease occurrence and fertility of dairy cows in three geographic regions of Chile. Theriogenology 86 (2016), 817–823.

Rajala-Schultz, P.J., Grohn, Y.T., 1999. Culling of dairy cows. Part I. Effects of diseases on culling in Finnish Ayrshire cows. Prev. Vet. Med. 41, 195–208.

Ramos, J.M., Freire, A., 2006. Effect of the year, season and animal category on the incidence of lame cows under grazing conditions in Uruguay. In: XIV Int Symp and VI Conf in Lameness in Ruminants, Nov 8-11. Colonia, Uruguay, pp. 78–79.

Reinhardt, T.A., Lippolis, J.D., McCluskey, B.J., Goff, J.P., Horst, R.L., 2011. Prevalence of subclinical hypocalcemia in dairy herds. Vet. J. 188, 122–124.

Ribeiro, E.S., Lima, F.S., Greco, L.F., Bisinotto, R.S., Monteiro, A.P.A., Favoreto, M., Ayres, H., Marsola, R.S., Martinez, N., Thatcher, W.W., Santos, J.E.P., 2013. Prevalence of periparturient diseases and effects on fertility of seasonally calving grazing dairy cows supplemented with concentrates. J. Dairy Sci. 96, 5682–5697.

Richardet, M., Castro, S., Tirante, L., Vissio, C., Larriestra, A.J., 2016. Magnitude and variation of clinical mastitis and its associated costs in dairy herds of Argentina. Arch. Med. Vet. 48, 153–158.

Robbins, J.A., von Keyserlingk, M.A.G., Fraser, D., Weary, D.M., 2016. Invited Review: farm size and animal welfare. J. Anim. Sci. 94, 5439–5455.

Rollin, E., Dhuyvetter, K.C., Overton, M.W., 2015. The cost of clinical mastitis in the first 30 days of lactation: an economic modeling tool. Prev. Vet. Med. 122, 257–264.

Ruegg, P.L., 2009. Implementing effective milk quality programmes. Ir. Vet. J. 62 (6), 411–415.

Ruprechter, G., Adrien, M.L., Larriestra, A., Meotti, O., Batistae, C., Meikle, A., Noro, M., 2018. Metabolic predictors of peri-partum diseases and their association with parity in dairy cows. Res. Vet. Sci. 118, 191–198.

Rutherford, K.M.D., Langford, F.M., Jack, M.C., Sherwood, L., Lawrence, A.B., Haskell, M.J., 2009. Lameness prevalence and risk factors in organic and non-organic dairy herds in the United Kingdom. Vet. J. 180, 95–105.

Santos, J.E.P., Cerri, R.L.A., Ballou, M.A., Higginbotham, G.E., Kirk, J.H., 2004. Effect of timing of first clinical mastitis occurrence on lactational and reproductive performance of Holstein dairy cows. Anim. Reprod. Sci. 80 (2004), 31–45.

Seegers, H., Beaudeau, F., Fourichon, C., Bareille, N., 1998. Reasons for culling in French Holstein cows. Prev. Vet. Med. 36, 257–271.

Sepúlveda Varas, P., Wittwer Menge, F., 2017. Transition Period: Importance in Health and Welfare of Dairy Cows, first edition. Sepúlveda Varas P. Chile.

Sepúlveda Varas, P., Weary, D.M., Noro, M., von Keyserlingk, M.A.G., 2015. Transition diseases in grazing dairy cows are related to serum cholesterol and other analytes. PLoSONE 10 (3), 0122317. https://doi.org/10.1371/journal.pone.0122317.

Shahid, M.Q., Reneau, J.K., Chester-Jones, H., Chebel, R.C., Endres, M.I., 2015. Cow and herd-level risk factors for on-farm mortality in Midwest US dairy herds. J. Dairy Sci. 98, 4401–4413.

Sheldon, I.M., Noakes, D.E., Rycroft, A.N., Pfeiffer, D.U., Dobson, H., 2002. Influence of uterine bacterial contamination after parturition on ovarian dominant follicle selection and follicle growth and function in cattle. Reproduction 123 (2002), 837–845.

Sheldon, I.M., Lewis, G.S., LeBlanc, S., Gilbert, R.O., 2006. Defining postpartum uterine disease in cattle. Theriogenology 65, 1516–1530.

Silva del Río, N., Stewart, S., Rapnicki, P., Chang, Y.M., Fricke, P.M., 2007. An observational analysis of twin births, calf sex ratio, and calf mortality in holstein dairy cattle. J. Dairy Sci. 90, 1255–1264.

Smith, J.W., Ely, L.O., Chapa, A.M., 2000. Effect of region, herd size, and milk production on reasons cows leave the herd. J. Dairy Sci. 83, 2980–2987.

Soto, P., Natzke, R.P., Hansen, P.J., 2003. Actions of tumor necrosis factor-a on oocyte maturation and embryonic development in cattle. Am. J. Reprod. Immunol. 50, 380–388.

Stevenson, M.A., 2000. Disease incidence in dairy herds in the southern highlands district of New South Wales, Australia. Prevent. Veterinary Med. 43, 1–11.

Stevenson, M.A., Lean, I.J., 1998. Descriptive epidemiological study on culling and deaths in eight dairy herds. Aust. Vet. J. 76, 7.

Suriyasathaporn, W., Heuer, C., Noordhuizen-Stassen, E.N., Schukken, Y.H., 2000. Hyperketonemia and the impairmentof udder defense: a review. Vet. Res. 31, 397–412.

Suthar, V.S., Canelas-Raposo, J., Deniz, A., Heuwieser, W., 2013. Prevalence of subclinical ketosis and relationships with postpartum diseases in European dairy cows. J. Dairy Sci. 96, 2925–2938.

Toni, F., Vincenti, L., Ricci, A., Schukken, Y.H., 2015. Postpartum uterine diseases and their impacts on conception and days open in dairy herds in Italy. Theriogenology 84, 1206–1214.

Verkerk, G.A., Hemsworth, P.H., 2010. Managing cow welfare in large dairy herds. In: Proceedings of the Australasian Dairy Science Symposium, Proceedings of the 4th Australasian Dairy Science Symposium. Aug. Publisher: Caxton Press.

Washburn, S.P., White, S.L., Green, J.T.J., Benson, G.A., 2002. Reproduction, mastitis, and body condition of seasonally calved holstein and jersey cows in confinement or pasture systems. J. Dairy Sci. 85, 105–111.

Wells, P.W., Burrells, C., Martin, W.B., 1977. Reduced mitogenic responses in cultures of lymphocytes from newly calved cows. Clin. Exp. Immunol. 29, 159–161.

Wells, S.J., Trent, A.M., Marsh, W.E., McGovern, P.G., Robinson, R.A., 1993. Prev. Vet. Med. 17, 95–109.