Preventive Veterinary Medicine 144 (2017) 7–12

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

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

Contextual herd factors associated with cow culling risk in Québec dairy herds: A multilevel analysis

Denis Haine[a,*], Hector Delgado[b], Roger Cue[b], Asheber Sewalem[c], Kevin Wade[b], René Lacroix[b,d], Daniel Lefebvre[b,d], Julie Arsenault[a], Émile Bouchard[a], Jocelyn Dubuc[a]

[a] Faculté de médecine vétérinaire, Université de Montréal, 3200 rue Sicotte, C.P.5000, St-Hyacinthe, Québec, Canada J2S 7C6
[b] Department of Animal Science, McGill University, 21111 Lakeshore Road, Ste-Anne-de-Bellevue, Québec, Canada H9X 3V9
[c] Guelph Food Research Centre, Agriculture and Agri-Food Canada, 93 Stone Road West, Guelph, Ontario, Canada N1G 5C9
[d] Valacta Inc., 555 boul. des Anciens-Combattants, Ste-Anne-de-Bellevue, Québec, Canada H9X 3R4

ARTICLE INFO

Article history:
Received 23 December 2016
Accepted 13 May 2017

Keywords:
Culling
Dairy cow
Multilevel
Contextual

ABSTRACT

Several health disorders, such as milk fever, displaced abomasum, and mastitis, as well as impaired reproductive performance, are known risk factors for the removal of affected cows from a dairy herd. While cow-level risk factors are well documented in the literature, herd-level associations have been less frequently investigated. The objective of this study was to investigate the effect of cow- and herd-level determinants on variations in culling risk in Québec dairy herds: whether herd influences a cow's culling risk. For this, we assessed the influence of herd membership on cow culling risk according to displaced abomasum, milk fever, and retained placenta.

A retrospective longitudinal study was conducted on data from dairy herds in the Province of Québec, Canada, by extracting health information events from the dairy herd health management software used by most Québec dairy producers and their veterinarians. Data were extracted for all lactations starting between January 1st and December 31st, 2010. Using multilevel logistic regression, we analysed a total of 10,529 cows from 201 herds that met the inclusion criteria. Milk fever and displaced abomasum were demonstrated to increase the cow culling risk. A minor general herd effect was found for the culling risk (i.e. an intra-class correlation of 1.0% and median odds ratio [MOR] of 1.20). The proportion of first lactation cows was responsible for this significant, but weak herd effect on individual cow culling risk, after taking into account the cow-level factors. On the other hand, the herd's average milk production was a protective factor. The planning and management of forthcoming replacement animals has to be taken into consideration when assessing cow culling risks and herd culling rates.

1. Introduction

Several health disorders, such as milk fever, displaced abomasum, and mastitis, as well as impaired reproductive performance, are known risk factors for the subsequent removal from a dairy herd of the affected animals (Gröhn et al., 1998; Rajala-Schultz and Gröhn, 1999; Beaudeau et al., 2000; De Vries et al., 2010). High culling rates can sometimes be viewed as a sign of management failure (Eicker and Fetrow, 2003) despite the lack of consensus on an acceptable culling rate, each herd having an optimal culling rate for its own management and dynamics (Rapnicki et al., 2003). Nevertheless, culling rates greater than 30% are common in American and Canadian dairy herds (Fetrow, 1987; Radke and Lloyd, 2000; Smith et al., 2000), despite improvements in cows' health and herd productivity (LeBlanc et al., 2006; Mee, 2007). While cow-level culling risk factors are well documented in the literature, herd-level associations have been less frequently investigated. But even without having this specific objective in mind, a significant herd effect on cow culling risk was reported by some studies (Beaudeau et al., 1995; Emanuelson and Oltenacu, 1998; Gröhn et al., 1998). The farmer's management style and attitude were shown to contribute significantly to the variation in farms' performance (Bigras-Poulin et al., 1985; Tarabla and Dodd, 1990). It is also recognized that group- or herd-level variables can affect or modify individual-level outcomes independently of the characteristics of the individuals (Diez Roux, 1998). Therefore we could hypothesize that several herd characteristics can modify the cow culling risk, such as suggested by Beaudeau et al. (2000): the availability of

---

[*] Corresponding author.
E-mail address: denis.haine@umontreal.ca (D. Haine).

http://dx.doi.org/10.1016/j.prevetmed.2017.05.014
0167-5877/

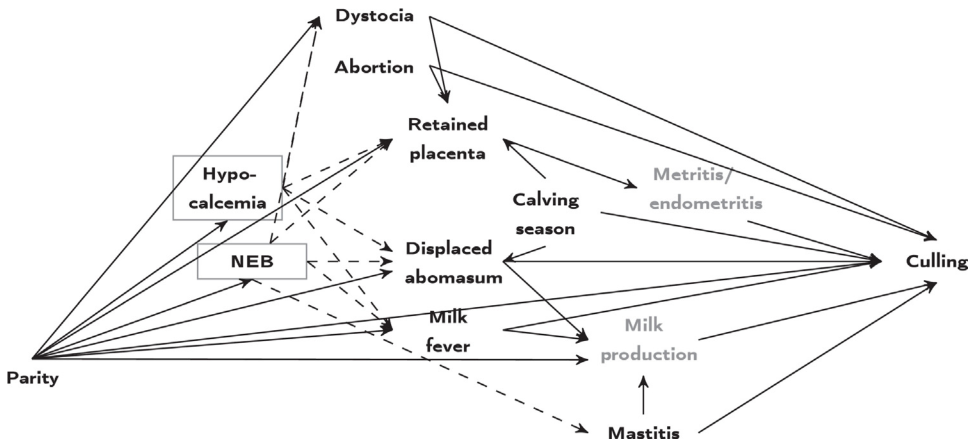

Fig. 1. Directed acyclic graph (DAG) for the effect of retained placenta, milk fever, and displaced abomasum on culling (grey: intermediate variables; boxes/dashed lines: unobserved [latent] variables; NEB: negative energy balance).

nulliparous heifers and milk quotas, the farmer's attitude towards risk and uncertainty, the milk and beef market, etc. Hence it would be interesting to integrate the population context into individual-level analyses to untangle the relationships between the variables at various levels (Guthrie and Sheppard, 2001), which has not yet been done in dairy cow culling research. Multilevel models achieve this goal by decomposing the variability across hierarchical levels (Stryhn and Christensen, 2014).

The objective of this study was to investigate the effect of herd-level determinants on variations in cow culling risk in Québec dairy herds, i.e. to examine whether, over and above cow factors, herd influences a cow's culling risk. To this end, we assessed and used the effect of retained placenta (RP), milk fever (MF), and displaced abomasum (DA) on culling.

2. Materials and methods

2.1. Dataset

A retrospective longitudinal study was conducted using data from dairy herds in the Province of Québec, Canada, by extracting health information events from *DSA Laitier* (DSAHR Inc., Saint-Hyacinthe, QC, Canada), the dairy herd health management software used by more than half of Québec producers and their veterinarians. We had access to a purposive sample of all lactations taking place between January 1st, 2001 and December 31st, 2010 (249,536 cows from 3735 herds), keeping herds that had a minimum of three consecutive years of data with *DSA Laitier* and for which at least one culling was recorded over this period. From this dataset, we extracted the data for all lactations starting between January 1st and December 31st, 2010. If a cow had more than two lactations starting in 2010, only the first was kept. Production data were obtained from the sole Québec dairy herd improvement (DHI) service provider (Valacta, Sainte-Anne-de-Bellevue, QC, Canada). The health and production data were matched based on herd- and cow-level identification. If that was not successful, further matching within herd was tried, based on birth date, calving dates, and health and production history. Only herds for which at least 95% of the lactations from the health dataset could be matched with data from the production dataset were kept (42,809 cows from 714 herds). Herds with fewer than 30 animals, for which more than 30% of the DHI monthly tests were missing, and with a 2010 lactational incidence that was less than 3% for RP, and 1% for either MF or DA, were removed to avoid herds with gross under-reporting. Cows with a calving interval, or the interval between the last calving and the end of data, longer than 580 days were censored at their last calving date. If this censoring resulted in their first calving date, the observation was dropped.

The primary outcome, culling, was defined as a cow's being removed from the herd, i.e. due to death, sold to another herd, or sent for slaughter. A directed acyclic graph (DAG, Fig. 1) was used to identify a minimal set of measured confounders for each disease studied (RP, MF, DA) (Greenland et al., 1999; Shrier and Platt, 2008), with the help of DAGitty software (Textor et al., 2011). Its construction was based on empirical knowledge from the findings of previous studies and on the authors' educated knowledge. This resulted in a single common DAG for the three diseases, with the following confounders considered: clinical mastitis, parity (continuous), calving season (January to July and August to December), dystocia, and abortion.

Six variables describing herd characteristics were included as contextual variables based on Haine et al. (submitted for publication): herd size, proportion of primiparous cows, average age at first calving, average milk production, milk fever incidence, and pregnancy rate.

2.2. Data analysis

The data were analysed using a two-level logistic regression model with cows (first level) nested within herds (second level). The independent influence of cow factors and herd factors on the herd variance of culling was assessed using different models. We first estimated an 'empty' model (Model 1) with no variables entered and which only included a random intercept. We then adjusted the random intercept by adding cow-level factors in Model 2. Herd-level predictors (Model 3) were added to Model 2 to determine whether the cow-level differences were explained by herd characteristics (Merlo et al., 2005). The random inter-herd variability was estimated by the herd-level variance, the intra-cluster correlation coefficient (ICC), and the median odds ratio (MOR). The ICC was calculated based on the latent response formulation as follows:

$$\frac{\sigma_z^2}{\sigma_z^2+(\pi^2/3}) \times 100 \tag{1}$$

where σ_z^2 is the herd variance (Goldstein et al., 2002; Snijders and Bosker, 2012). The ICC indicates the fraction of the total outcome variability that is attributable to the herd level and provides a measure of the within-herd homogeneity. A lower ICC indicates a lower likelihood of cows' sharing herd experiences. However, the ICC can

Table 1
Characteristics of cows by culling status (201 herds).

	Non-culled $N = 7991$	Culled $N = 2538$	Total $N = 10{,}529$
Parity			
1	2609 (33%)	607 (24%)	3216 (31%)
2	2082 (26%)	472 (19%)	2554 (24%)
3	1458 (18%)	456 (18%)	1914 (18%)
4+	1842 (23%)	1003 (40%)	2845 (27%)
Age at first calving (months)			
<24	1115 (15%)	347 (15%)	1462 (15%)
24–26	3270 (43%)	940 (41%)	4210 (43%)
26–28	1836 (24%)	582 (25%)	2418 (24%)
>28	1363 (18%)	437 (19%)	1800 (18%)
305-day milk production, kg (SD)[a]	9865 (±1919)	9875 (±1957)	9866 (±1921)
Milk fever	286 (4%)	219 (9%)	505 (5%)
Displaced abomasum	339 (4%)	145 (6%)	484 (5%)
Dystocia	635 (8%)	290 (11%)	925 (9%)
Abortion	158 (2%)	125 (5%)	283 (3%)
Retained placenta	592 (7%)	244 (10%)	836 (8%)
Calved, August to December	2,878 (36%)	945 (37%)	3823 (36%)

[a] Mean, based on real production; SD = standard deviation; non available for 1418 non-culled and 2185 culled cows.

be difficult to interpret with binary outcomes, as the partition of the variance between the different levels does not have the intuitive interpretation of a linear model (Goldstein et al., 2002). Therefore we also calculated the MOR, defined as the median value of the odds ratio between the herd at highest risk (higher culling rate) and the herd at lowest risk when randomly picking out two herds (Larsen et al., 2000). The MOR can be conceptualized as the increased risk (in median) that a cow would have if moved to a herd with a higher risk. It is statistically independent of the prevalence of culling and is also the most appropriate indicator for measuring the variation for dichotomous outcomes compared to ICC, which varies as a function of the prevalence and has serious interpretational drawbacks for binary responses (Merlo et al., 2006). The values of MOR are always ≥1. If the MOR is equal to 1, then there is no variation in the probability of being culled between herds, whereas a value greater than 1 indicates that there is a variation in the probability of being culled between herds – the larger the odds ratio (OR), the greater the variation (Larsen and Merlo, 2005; Merlo et al., 2006). In addition, we also calculated the percentage of proportional change in variance (PCV) between two consecutive models to examine the extent to which the variables explain the variation in culling across herds.

The culling incidence was computed using a generalized estimating equation (GEE) model (Yan and Fine, 2004; Højsgaard et al., 2006) with Poisson distribution, log link function, exchangeable correlation structure, and robust sandwich estimator.

The parameters for the multilevel logistic regression models were estimated using Markov Chain Monte Carlo (MCMC), implemented using the Stan (Carpenter et al., 2017) modelling language through the rstan (Stan Development Team, 2016) interface to R (R Core Team, 2015). This software implements Hamiltonian MCMC using the 'No U-turn' sampler (Hoffman and Gelman, 2014), an MCMC algorithm that avoids random walk behaviour by using the gradient of the log-posterior (Neal, 2011). Each MCMC sample used four sampling chains with 100 burn-in samples followed by 900 monitored samples. We checked for evidence of non-convergence using trace plots and the chain convergence indicator $\hat{R}$ (Gelman et al., 2014). The model adjustments were assessed using the Watanabe–Akaike Information Criterion (WAIC; Watanabe, 2010). The models were run under the Amazon EC2 cloud-computing environment (one node with a quad-core Intel(R) Xeon(R) CPU E5-2670 v2 and Ubuntu Server 14.04 LTS 64-bit operating system). The effect of potential selection bias was checked with the R episensr package in a probabilistic framework (Haine, 2016). Selection odds ratios were computed for RP, MF, and DA based on the selection proportion for each exposure from the non-selected observations of the database (Lash et al., 2009). We assumed that the bias parameters were drawn from a trapezoidal distribution with minimum, lower mode, upper mode, and maximum equal to the selection OR minus 0.25, minus 0.2, plus 0.2, and plus 0.25, respectively. We used 100,000 repetitions to randomly sample the selection OR to obtain estimates of the back-calculated ORs for comparison with the original, crude ORs.

3. Results

Table 1 presents the characteristics of the 10,529 cows from 201 herds that met the inclusion criteria. The median herd lactational incidence risks were 4.2%, 3.4%, and 7.1% for DA, MF, and RP, respectively. Herd sizes ranged from 31.9 to 302.9 cow-years (median: 58.1). Information on breed was sparse in the database, but we estimated that at least 90% of the cows were Holsteins. The culling incidence rate and 95% confidence interval (CI) were 30.3 culled cows per 100 cow-year [28.8–31.8].

Table 2 gives the OR and their 95% credible intervals (CrI) for the cow-level and contextual (herd-level) characteristics from the three models used. With cow- and herd-level variables controlled for, there was no difference between cows having or not RP on the risk of being culled with an OR and 95% CrI of 1.12 [0.96–1.31]. The two other diseases, MF and DA, were significantly associated with culling (OR and CrI of 1.85 [1.52–2.24] and 1.31 [1.07–1.62], respectively). The probability of a cow's being culled increased with parity (OR = 1.23 [1.19–1.26]). With the exception of calving season, all other cow-level confounding variables had a significant direct effect on culling. Cows having clinical mastitis had a higher probability of being culled, by about 40%. Dystocia and abortion also increased the odds of culling. Two herd-level variables showed a significant effect: the proportion of first lactation cows in the herd, and the average herd milk production. Over and above the cow characteristics (presence of RP, MF, DA, clinical mastitis, dystocia or abortion, parity, and time of calving), being in a herd with a large proportion of primiparous cows increased a cow's probability of being culled (OR = 1.35 [1.16–2.59]). Similarly, a cow in a relatively high producing herd has a slightly lower probability of being culled (OR = 0.83 [0.71–0.98]). However, the relationship is less clear in very high producing herds (top quartile of herd average production in Table 2; OR = 0.89 [0.76–1.05]). The associations between the cow variables and culling were rather similar in all models (i.e. 2 and 3).

Table 2
Multilevel logistic models showing variance, cow- and herd-level predictors for retained placenta, milk fever, and displaced abomasum ($n = 10{,}529$; 201 herds).

	Model 1[a]		Model 2[b]		Model 3[c]	
	OR	95% CrI	OR	95% CrI	OR	95% CrI
Fixed effects						
Cow level						
Retained placenta			1.12	0.94, 1.32	1.12	0.96, 1.31
Milk fever			1.85	1.53, 2.24	1.85	1.52, 2.24
Displaced abomasum			1.31	1.06, 1.59	1.31	1.07, 1.62
Clinical mastitis			1.40	1.24, 1.58	1.39	1.23, 1.57
Parity			1.22	1.19, 1.25	1.23	1.19, 1.26
Calving, August to December			1.09	0.99, 1.19	1.09	0.99, 1.2
Dystocia			1.59	1.37, 1.84	1.59	1.36, 1.85
Abortion			2.81	2.2, 3.61	2.81	2.2, 3.63
Herd level						
Herd size						
1st quartile (smallest)					Ref.	
2nd quartile					1.03	0.86, 1.24
3rd quartile					1.04	0.87, 1.24
4th quartile (largest)					1.02	0.86, 1.22
Proportion of primiparous						
1st quartile (lowest)					Ref.	
2nd quartile					1.13	0.96, 1.33
3rd quartile					1.22	1.03, 1.44
4th quartile (highest)					1.35	1.16, 1.59
Average age at first calving						
1st quartile (youngest)					Ref.	
2nd quartile					1.09	0.93, 1.28
3rd quartile					1.08	0.91, 1.27
4th quartile (oldest)					1.01	0.85, 1.2
Average milk production						
1st quartile (lowest)					Ref.	
2nd quartile					0.83	0.71, 0.98
3rd quartile					0.83	0.71, 0.98
4th quartile (highest)					0.89	0.76, 1.05
Milk fever incidence						
1st quartile (lowest)					Ref.	
2nd quartile					0.91	0.78, 1.07
3rd quartile					1.00	0.85, 1.18
4th quartile (highest)					1.00	0.85, 1.18
Pregnancy rate						
1st quartile (lowest)					Ref.	
2nd quartile					1.06	0.9, 1.25
3rd quartile					1.02	0.86, 1.2
4th quartile (highest)					1.04	0.88, 1.23
Random effect						
Variance	0.038	0.014, 0.07	0.054	0.025, 0.09	0.043	0.013, 0.079
PCV (%)			43		−21	
ICC (%)	1.0	0.4, 1.9	1.4	0.7, 2.4	1.1	0.4, 2.1
MOR	1.20	1.12, 1.29	1.25	1.16, 1.33	1.22	1.12, 1.31
WAIC	11,612		11,184		11,192	
WAIC change			−429		9	

OR, odds ratio; CrI, credible interval; PCV, proportional change of herd variance; ICC, intraclass correlation coefficient; MOR, median odds ratio; WAIC, Watanabe–Akaike information criteria.

[a] Empty model.

[b] With cow-level variables.

[c] With contextual variables.

In Model 1 (the empty model), there was a significant variation in the log odds of culling across herds ($\sigma^2 = 0.038$, 95% CrI 0.014–0.07). According to the ICC implied by the estimated intercept component variance, 1.0% of the total cow differences in culling risk were at the herd level. Model 2 indicates that over and above the cow characteristics only 1.4% of the total cow differences in the propensity of being culled were at the herd level. Variations across herds remained statistically significant, even after controlling for cow-level and herd-level factors in the final Model 3, thereby giving credence to the use of multilevel modelling to account for herd variations. In Model 2, ICC and MOR were weak (1.4% and 1.25, respectively) which indicate that the herd captures some context for understanding a cow's probability of being culled. Taking into account the individual characteristics of the cows in Model 2 increased the herd variance. According to the proportional change in variance, about 21% of the variance in the log odds of culling across the herds were explained by the herd-level factors (Model 3).

The MOR results also confirmed the evidence of a herd contextual phenomena modifying the likelihood of a cow's being culled. In the median case, if a cow is moved to a herd with a greater risk of culling, the OR will be 1.20, which suggests a limited heterogeneity between herds. Controlling for cow-level factors increased the unexplained heterogeneity between herds to an MOR of 1.25. The unexplained herd heterogeneity decreased to 1.22 when all the factors were controlled for in the final Model 3. Thus, between herd variations in the likelihood of being culled are present, but these variations are small.

In assessing the model adjustment, we observed reduced WAIC values after including contextual-level variables. All models converged quickly and every $\hat{R}$ was below 1.01.

Selection ORs were 1.0, 1.08, and 0.96 for RP, DA, and MF, respectively. Adjusted crude ORs were equivalent to the non-adjusted ones.

4. Discussion

It is usually acknowledged that RP has no effect by itself on culling likelihood (Gröhn et al., 1998; Dubuc et al., 2011), even if some studies report it as a risk factor (Beaudeau et al., 1994). Rather, it is a risk factor for metritis and endometritis (LeBlanc, 2008), resulting in negative effects on reproductive performance (Fourichon et al., 2000; Gröhn and Rajala-Schultz, 2000; Dubuc et al., 2010). We demonstrated here the non-significant total effect of RP on culling risk. On the other hand, DA and MF are known risk factors for culling (Beaudeau et al., 1994; Gröhn et al., 1998; Hayes et al., 2012), and this study was no exception. More interesting was the exploration of a potential herd contextual effect on the culling risk. Although we found a significant variation between herds, this observed general contextual effect was fairly small (i.e. 1.0%). The addition of the contextual characteristics explained 21% of the herd variance, but variance was small (i.e. $\sigma^2 = 0.043$). Therefore it explains a substantial amount of a small effect. However, as the ICC and the partition of variance between different levels do not have the same intuitive interpretation as in linear models (Goldstein et al., 2002), we can refer to the MOR for exploring herd variation. None of the MOR credible intervals for the various models included 1. So there was a herd effect on culling rate. However, the herd effect was limited, as illustrated by a low MOR of 1.22. Even if small, we found a positive association between the selected herd characteristics and cow culling, over and above the cow's individual risk, possibly resulting from the pressure applied by the incoming flow of heifers on the herd size to remain constant. On the other hand, average herd milk production served as a protective factor for cow culling risk. However, when reaching a certain production threshold, the need to produce in these high-producing herds establishes an increasing pressure on the cows.

Replacement heifers are generally raised on farms in the Québec dairy herd management system. For a herd with good reproductive performance (i.e. 13 month calving interval) and heifer rearing program (i.e. low mortality, first calving around 24 months of age), around 40% of the herd will have a female calf reaching the milk production stage (Eicker and Fetrow, 2003). In other words, a herd culling rate of 40%. All herd managers therefore face the same decision: a choice has to be made between the next heifers to come into the herd, and the least profitable cow. Having little variation between herds (i.e. cow culling risk being rather uniform across herds), implies there is no characteristic, or target, herd for lowering the herd culling rate. Once individual risk factors are managed for the cows, all herds would benefit from a comprehensive evaluation of the replacement heifer strategy. However, even though the herd variation was small, a relatively large amount of variation was still not explained by the contextual variables introduced in the model. Other factors might be at play, including dairy producers' perceptions of risk, and personal management preferences and styles (Bigras-Poulin et al., 1985).

Potential biases might have hindered this study. However, herds were deemed representative of Québec dairy herds using a monthly DHI service for individual cow milk recording, and a computerized data management system for reproduction and health management. The incidences of DA, MF, and RP in this study were in line with what has been reported previously in the literature (Kelton et al., 1998; Fleischer et al., 2001; Dubuc et al., 2010). The herds were selected based on the availability of comprehensive health event records. If under-reporting bias is then minimized, a selection bias could have been introduced. By comparing the selection probability within levels of the exposure, the probabilistic sensitivity analysis gave about the same ORs and confidence intervals. We therefore have good confidence in the validity of our results.

5. Conclusion

We found a significant but limited herd effect on individual cow culling risk. Any attempt to manage the cull rate with the objective of decreasing it will have to take into account the improvement of both cow and herd health, including reproduction management and milk production planning and quality assessment. However the incoming flow of heifers should not be forgotten, i.e. planning and managing the forthcoming replacement animals.

Conflict of interest

None.

Acknowledgements

The authors thank Agriculture and Agri-Food Canada, Fonds de recherche du Québec – Nature et technologies (FQRNT), Novalait, and Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec (MAPAQ) for supporting this study (grant LT-163341).

References

Beaudeau, F., Ducrocq, V., Fourichon, C., Seegers, H., 1995. Effect of disease on length of productive life of French Holstein dairy cows assessed by survival analysis. J. Dairy Sci. 78 (1), 103–117 http://www.sciencedirect.com/science/article/pii/S0022030295766218.

Beaudeau, F., Frankena, K., Fourichon, C., Seegers, H., Faye, B., Noordhuizen, J.P.T.M., 1994. Associations between health disorders of French dairy cows and early and late culling within the lactation. Prev. Vet. Med. 19 (3–4), 213–231 http://www.sciencedirect.com/science/article/pii/0167587794900906.

Beaudeau, F., Seegers, H., Ducrocq, V., Fourichon, C., Bareille, N., 2000. Effect of health disorders on culling in dairy cows: a review and a critical discussion. Ann. Zootech. 49, 293–312 http://prodinra.inra.fr/record/4291.

Bigras-Poulin, M., Meek, A.H., Martin, S.W., McMillan, I., 1985. Attitudes, management practices, and herd performance – a study of Ontario dairy farm managers. II. Associations. Prev. Vet. Med. 3 (3), 241–250 http://www.sciencedirect.com/science/article/pii/0167587785900194.

Carpenter, B., Gelman, A., Hoffman, M., Lee, D., Goodrich, B., Betancourt, M., Brubaker, M.A., Li, P., Riddell, A., 2017. Stan: a probabilistic programming language. J. Stat. Softw. 76, 1–32, http://dx.doi.org/10.18637/jss.v076.i01.

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 (2), 613–623.

Diez Roux, A.V., 1998. Bringing context back into epidemiology: variables and fallacies in multilevel analysis. Am. J. Public Health 88 (2), 216–222, http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.88.2.216.

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 (12), 5764–5771 http://www.ncbi.nlm.nih.gov/pubmed/21094748.

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 (3), 1339–1346 http://www.sciencedirect.com/science/article/pii/S0022030211000889.

Eicker, S., Fetrow, J., 2003. A prospective view of culling. In: 2003 Midwest Dairy Herd Health Conference. University of Wisconsin-Madison, Madison.

Emanuelson, U., Oltenacu, P.A., 1998. Incidences and effects of diseases on the performance of Swedish dairy herds stratified by production. J. Dairy Sci. 81, 2376–2382, http://dx.doi.org/10.3168/jds.S0022-0302(98)70129-8.

Fetrow, J., 1987. Culling dairy cows. In: 20th Annual Convention Proceedings, AABP, Phoenix, AZ, pp. 102–107.

Fleischer, P., Metzner, M., Beyerbach, M., Hoedemaker, M., Klee, W., 2001. The relationship between milk yield and the incidence of some diseases in dairy cows. J. Dairy Sci. 84 (9), 2025–2035 http://www.sciencedirect.com/science/article/pii/S0022030201746462.

Fourichon, C., Seegers, H., Malher, X., 2000. Effect of disease on reproduction in the dairy cow: a meta-analysis. Theriogenology 53 (9), 1729–1759 http://www.sciencedirect.com/science/article/pii/S0093691X00003113.

Gelman, A., Carlin, J.B., Stern, H.S., Dunson, D.B., Vehtari, A., Rubin, D.B., 2014. Bayesian Data Analysis, 3rd ed. Chapman & Hall/CRC, Boca Raton, FL.

Goldstein, H., Browne, W., Rasbash, J., 2002. Partitioning variation in multilevel models. Understand. Stat. 1 (4), 223–231.

Greenland, S., Pearl, J., Robins, J.M., 1999. Causal diagrams for epidemiologic research. Epidemiology 10 (1), 37–48 http://www.ncbi.nlm.nih.gov/pubmed/9888278.

Gröhn, 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 (4), 966–978 http://www.sciencedirect.com/science/article/pii/S0022030298756577.

Gröhn, Y.T., Rajala-Schultz, P.J., 2000. Epidemiology of reproductive performance in dairy cows. Anim. Reprod. Sci. 60–61 (0), 605–614 http://www.sciencedirect.com/science/article/pii/S0378432000000853.

Guthrie, K.A., Sheppard, L., 2001. Overcoming biases and misconceptions in ecological studies. J. R. Stat. Soc. Ser. A 164 (1), 141–154.

Haine, D., 2016. episensr: Basic sensitivity analysis of epidemiological results. R package version 0.8.0. https://cran.r-project.org/web/packages/episensr/.

Haine, D., Delgado, H., Cue, R., Sewalem, A., Wade, K., Lacroix, R., Lefebvre, D., Rushton, J., Arsenault, J., Bouchard, E., Dubuc, J., 2017. Culling from a herd's perspective–Exploring herd-level management factors and culling rates in Québec dairy herds. Prev. Vet. Med. (submitted for publication).

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 (21), 540, http://veterinaryrecord.bmj.com/cgi/doi/10.1136/vr.100317.

Højsgaard, S., Halekoh, U., Yan, J., 2006. The R package GEEPACK for generalized estimating equations. J. Stat. Softw. 15 (2), 1–11.

Hoffman, M.D., Gelman, A., 2014. The No-U-Turn Sampler: adaptively setting path lengths in Hamiltonian Monte Carlo. J. Mach. Learn. Res. 15 (April), 1593–1623 http://mc-stan.org/.

Kelton, D.F., Lissemore, K.D., Martin, R.E., 1998. Recommendations for recording and calculating the incidence of selected clinical diseases of dairy cattle. J. Dairy Sci. 81 (9), 2502–2509 http://www.sciencedirect.com/science/article/pii/S0022030298701420.

Larsen, K., Merlo, J., 2005. Appropriate assessment of neighborhood effects on individual health: integrating random and fixed effects in multilevel logistic regression. Am. J. Epidemiol. 161 (1), 81–88.

Larsen, K., Petersen, J.H., Budtz-Jørgensen, E., Endahl, L., 2000. Interpreting parameters in the logistic regression model with random effects. Biometrics 56 (September), 909–914.

Lash, T.L., Fox, M.P., Fink, A.K., 2009. Applying Quantitative Bias Analysis to Epidemiologic Data. Springer http://www.springer.com/public+health/book/978-0-387-87960-4.

LeBlanc, S.J., 2008. Postpartum uterine disease and dairy herd reproductive performance: a review. Vet. J. 176 (1), 102–114, http://dx.doi.org/10.1016/j.tvjl.2007.12.019.

LeBlanc, S.J., 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 (4), 1267–1279 http://www.sciencedirect.com/science/article/pii/S0022030206721956.

Mee, J.F., 2007. The role of the veterinarian in bovine fertility management on modern dairy farms. Theriogenology 68 (Suppl. 1), S257–S265 http://www.sciencedirect.com/science/article/pii/S0093691X0700177X.

Merlo, J., Chaix, B., Ohlsson, H., Beckman, A., Johnell, K., Hjerpe, P., Råstam, L., Larsen, K., 2006. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. J. Epidemiol. Community Health 60 (4), 290–297 http://jech.bmj.com/content/60/4/290.short.

Merlo, J., Chaix, B., Yang, M., Lynch, J., Råstam, L., 2005. A brief conceptual tutorial on multilevel analysis in social epidemiology: interpreting neighbourhood differences and the effect of neighbourhood characteristics on individual health. J. Epidemiol. Community Health 59 (12), 1022–1029, http://jech.bmj.com/cgi/doi/10.1136/jech.2004.028035.

Neal, R., 2011. MCMC Using Hamiltonian Dynamics. In: Brooks, S., Gelman, A., Jones, G.L., Meng, X.-L. (Eds.), Handbook of Markov Chain Monte Carlo. Chapman & Hall/CRC Press, pp. 113–162 (Chapter 5).

R Core Team, 2015. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria http://www.R-project.org.

Radke, B., Lloyd, J., 2000. Sixteen dairy culling and replacement myths. Compendium Continuing Educ. Pract. Vet., S36–S57 http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=caba5&AN=20002210649.

Rajala-Schultz, P.J., Gröhn, Y.T., 1999. Culling of dairy cows. Part I. Effects of diseases on culling in Finnish Ayrshire cows. Prev. Vet. Med. 41 (2–3), 195–208 http://www.sciencedirect.com/science/article/pii/S016758779900046X.

Rapnicki, P., Stewart, S., Fetrow, J., Eicker, S., 2003. 'Dead cows tell no . . .'. In: The North American Veterinary Conference 2003, Large Animal., pp. 18–22 http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=caba6&AN=20063003867.

Shrier, I., Platt, R.W., 2008. Reducing bias through directed acyclic graphs. BMC Med. Res. Methodol. 8 (1) http://www.biomedcentral.com/1471-2288/8/70/abstract.

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 (12), 2980–2987 http://www.sciencedirect.com/science/article/pii/S0022030200751988.

Snijders, T.A.B., Bosker, R.J., 2012. Multilevel Analysis. An Introduction to Basic and Advanced Multilevel Modeling, 2nd ed. SAGE Publications, London, UK.

Stan Development Team, 2016. RStan: the R interface to Stan. http://mc-stan.org.

Stryhn, H., Christensen, J., 2014. The analysis – hierarchical models: past, present and future. Prev. Vet. Med. 113 (3), 304–312 http://linkinghub.elsevier.com/retrieve/pii/S016758771300295X.

Tarabla, H.D., Dodd, K., 1990. Association between farmers' personal characteristics, management practices and farm performance. Br. Vet. J. 146, 157–165.

Textor, J., Hardt, J., Knüppel, S., 2011. DAGitty: a graphical tool for analyzing causal diagrams. Epidemiology 22 (5), 745.

Watanabe, S., 2010. Asymptotic equivalence of Bayes cross validation and Widely Applicable Information Criterion in singular learning theory. J. Mach. Learn. Res. 11, 3571–3594 http://www.jmlr.org/papers/volume11/watanabe10a/watanabe10a.pdf.

Yan, J., Fine, J.P., 2004. Estimating equations for association structures. Stat. Med. 23, 859–880.