

# Effect of Diseases on the Culling of Holstein Dairy Cows in New York State

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## ABSTRACT

The effect of seven diseases on culling was measured in 7523 Holstein cows in New York State. The cows were from 14 herds and had calved between January 1, 1994 and December 31, 1994; all cows were followed until September 30, 1995. Survival analysis was performed using the Cox proportional hazards model to incorporate time-dependent covariates for diseases. Different intervals representing stages of lactation were considered for effects of the diseases. Five models were fitted to test how milk yield and conception status modified the effect of diseases on culling. Covariates in the models included parity, calving season, and time-dependent covariates measuring diseases, milk yield of the current lactation, and conception status. Data were stratified by herd. The seven diseases and lactational risks under consideration were milk fever (0.9%), retained placenta (9.5%), displaced abomasum (5.3%), ketosis (5.0%), metritis (4.2%), ovarian cysts (10.6%), and mastitis (14.5%). Older cows were at a much higher risk of being culled. Calving season had no effect on culling. Higher milk yield was protective against culling. Once a cow had conceived again, her risk of culling dropped sharply. In all models, mastitis was an important risk factor throughout lactation. Milk fever, retained placenta, displaced abomasum, ketosis, and ovarian cysts also significantly affected culling at different stages of lactation. Metritis had no effect on culling. The magnitude of the effects of the diseases decreased, but remained important, when milk yield and conception status were included as covariates. These results indicated that diseases have an important impact on the actual decision to cull and the timing of culling. Parity, milk yield, and conception status are also important factors in culling decisions.

(**Key words:** time-dependent covariates, survival analysis, disease, culling)

**Abbreviation key:**  $-2\text{LOGL}$  =  $-2 \log$  likelihood, **RR** = risk ratio.

## INTRODUCTION

Culling is a complex issue, and many factors are involved. Dairy cows may be culled for either involuntary reasons (i.e., death, acute disease, infertility) or voluntary reasons (i.e., low yield). Both biology and management affect the decision to cull. When making a decision, the dairy farmer considers five major reasons: illness, low milk yield, conception status, stage of lactation, and parity. Culling potentially increases profits or reduces costs through the replacement of sick or open cows that are expensive to keep and may die or through the replacement of low yielding cows. The culling rate, which varies from herd to herd, depends on input and output prices, yields, seasonal variation of price, incidence of disease, and other variable factors (15, 19, 20, 21).

The primary interest of this study was the effect of several diseases (milk fever, retained placenta, displaced abomasum, ketosis, metritis, ovarian cysts, and mastitis) on culling. We postulated that diseases have both direct and indirect effects on culling (11). The indirect effects may be reflected in milk yield or even conception status. Lower yielding cows, whether diseased or not, are more likely to be culled. Conversely, high yielding cows, even if they are diseased, are more likely to be kept in the herd. Similarly, pregnant cows are more likely to remain in the herd than are open cows. To what extent diseases affect the culling process through lower milk yield or lower reproductive performance as measured by conception status is unclear. How the effect of disease may change through the inclusion of milk yield or conception status in the model was determined in this study.

Although several techniques have been used to study survival data [e.g., logarithm of odds ratios method (4), discriminant analysis (7), path analysis (10), logistic regression (12), path analysis combined with logistic regression (18)], survival analysis is now generally accepted as the most appropriate

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method. Survival analysis, which became widely known after Cox (5) developed the proportional hazards model, accounts for all subjects, even those that have not yet experienced the event of interest (in this study, culling). Such subjects are said to be censored; they are still alive (i.e., still at risk of being culled) at the end of the study. Other statistical techniques are not able to model such observations, which are simply dropped from the analysis, and important information is lost.

Diseases may have different effects on culling depending on when they occur and when the effect of the disease on culling is observed. In dairy cows, culling can occur throughout lactation. Similarly, some diseases, especially mastitis, can occur at any time during lactation. Therefore, erroneous conclusions may be drawn if diseases are considered to have only one effect (i.e., at only one point in time) on culling (1, 11). Time-dependent covariates address this problem because these values change depending on when they are observed. Only a few studies (1, 11) using survival analysis have incorporated the dependence on time of some covariates because the statistical techniques available were not yet capable of handling this complexity. Recently, however, it has become computationally possible to handle time-dependent covariates in survival analysis. The analyses in this study were conducted using The Survival Kit, a set of FORTRAN programs (8). These programs make it possible to account for the effect of a covariate, such as disease, during different periods of the study, such as stages of lactation, that are defined by the user. In a previous study (11), we described the methodological aspects involved in the estimation of the effect of mastitis on culling; mastitis was considered to be a time-dependent covariate. In that study, we determined that an interaction between time of mastitis occurrence and the time of actual culling was important. We, therefore, used this approach to study the effect of seven diseases on culling. The modifying effects of milk yield and conception status on the effect of diseases on culling were also studied, and the interactions between these covariates and stage of lactation were taken into account.

## MATERIALS AND METHODS

### Study Population

The data file consisted of 7523 Holstein cows from 14 herds in New York State. Cows calved between January 1, 1994 and December 31, 1994 and were followed until September 30, 1995. Data were obtained from on-farm software marketed and sup-

ported by the Northeast DHIA (Ithaca, NY). Data on cow and herd identification, calving and culling (or censoring) dates, parity, previous 305-d milk yield, and test day milk yields at 30, 60, 120, 180, and 240 d of the current lactation (based on interpolation using actual values from the nearest test day milk yield) were recorded. Dates of occurrence, if any, of milk fever, retained placenta, displaced abomasum, ketosis, metritis, ovarian cysts, mastitis, and subsequent conceptions, were also available. Dairy personnel entered all diagnoses into on-farm computers.

The dependent variable of interest was the number of days between calving and culling or censoring. A cow was considered to be culled if she left the herd because of death or sale for meat. In this study, only commercial dairies that did not market cows were included. A cow was considered to be censored if she began a new lactation during the study period; she was censored on her new calving date. A cow was also considered to be censored if she was still in the herd on the last day of the study period (September 30, 1995) and had not yet begun a new lactation.

Within each herd and parity, previous 305-d milk yields and the test day milk yields were divided into six categories. The category labeled "missing" represented cows (likely diseased; fewer than 40 out of 7523) that were missing a milk yield measurement but that were known to be in the milking herd at the time. The other five categories represented the lowest to the highest milk yields, divided into quintiles. Current milk yield was treated as a time-dependent covariate. For cows that were culled before 30 d of lactation, the value of the previous 305-d milk yield was assumed (for first parity cows, a separate category was created); the last known test day record (taken at 30, 60, 120, 180, and 240 d) was then used until the next one was available or until censoring or culling occurred. Milk yield was categorized to account for any nonlinear association between milk yield and culling. Parity was divided into six categories: parities one through five, and parity six or greater. The year was divided into four calving seasons: December through February, March through May, June through August, and September through November. Conception status was determined by rectal palpation. Although conception status was unknown until pregnancy was diagnosed, status was considered to change at the time of conception; therefore, a time-dependent covariate with two levels existed.

In the succession of events that relate disease and culling, two aspects should be considered: when the disease occurs and when the disease actually induces culling. Both aspects were tested and are accounted for in this study. In a previous study (11), we deter-

mined that this method was appropriate for modeling the effect of mastitis on culling. For each cow with a disease, it was of interest to see the effect of the disease on culling in different stages of lactation. For instance, displaced abomasum might be associated with an increased risk of culling immediately after the disease was diagnosed but might have very little effect as the lactation progresses. Time-dependent covariates allow the characterization of effects of each disease on culling depending both on the period in which the disease occurred and the stage of lactation at which the effect on culling was observed. Periods and stages (both defined in Table 1) were chosen based on results from preliminary models and the distribution of cullings for each disease throughout lactation. The distribution of cases of disease and by period of occurrence is also given in Table 1.

In all herds, some diseases were underreported; these diseases varied among herds. To determine whether such inaccuracies would affect the point estimates in the main model, we fitted models for each disease separately. In this preliminary analysis, only herds that had incidences of disease that were comparable with those of similar herds served by the Cornell Ambulatory Clinic (Cornell University, Ithaca, NY) were included in the model. The seven

preliminary models (one for each disease) consequently included a variable number of herds; all models included variables for parity, season, milk yield, and the disease in question. The inclusion of herds for which diseases were underreported did not change the estimates. Because the results were similar, we concluded that recording inaccuracies did not have a major effect on the estimates. Stratification by herd greatly reduces the problem of underreporting in the overall model estimates because disease effects appear to act additively on the log scale of the model (1) (i.e., multiplicatively on the hazard scale). Thus, one of these effects, if underreported, can be factored out and incorporated into the baseline hazard function for the herd. This procedure does not alter the other estimates. Essentially, the underreporting of diseases is a measurement error. However, the effect of including rare diseases in the healthy animal group has a minimal effect on the healthy cohort. Therefore, all results reported in this paper were derived from models including all 14 herds.

## Models

Cox proportional hazards regression models were fitted to the data; these models are ideal for this type

TABLE 1. The occurrence of diseases and the effects of disease on stage of lactation of 7523 Holstein dairy cows in New York State from calving in 1994 until September 30, 1995.<sup>1</sup>

	Milk fever	Retained placenta	Displaced abomasum	Ketosis	Metritis	Ovarian cysts	Mastitis
<b>Period of occurrence<sup>2</sup></b>							
1	As it occurs <sup>3</sup> (n = 70)	As it occurs (n = 714)	As it occurs (n = 402)	As it occurs (n = 379)	As it occurs (n = 316)	1-120 (n = 427)	1-60 (n = 587)
2	...	...	...	...	...	>120 (n = 367)	61-150 (n = 226)
3	...	...	...	...	...	...	151-270 (n = 203)
4	...	...	...	...	...	...	>270 (n = 72)
<b>Stage of lactation<sup>4</sup></b>							
1	1-30	1-30	1-30	1-30	1-60	1-60	1-30
2	31-240	31-240	31-60	31-120	61-240	61-240	31-60
3	>240	>240	61-120	121-180	>240	>240	61-120
4	...	...	121-180	181-240	...	...	121-180
5	...	...	181-240	>240	...	...	181-240
6	...	...	>240	...	...	...	>240

<sup>1</sup>Values are days of lactation; numbers in parentheses are cases of disease.

<sup>2</sup>Period of lactation during which disease occurred; periods were defined differently depending on when the disease under consideration could reasonably occur.

<sup>3</sup>Most cases of these diseases occurred very early in lactation and had only one period of occurrence. However, a few isolated cases occurred later in lactation, especially displaced abomasum, ketosis, and metritis.

<sup>4</sup>Stage of lactation during which culling occurred; stages were defined differently depending on the distribution of cullings throughout lactation for the disease under consideration.

of problem because they can accommodate time-dependent covariates. These models consisted of two parts: a baseline hazard function that was common to all observations and a vector of covariates for each individual observation. In this study, the data were stratified by herd (i.e., the baseline was different in each herd).

The proportional hazards model describes the hazard of some event (in this study, culling) at any time  $t$ :

$$\lambda[t; \mathbf{x}, \mathbf{z}(t)] = \lambda_0(t) \exp[\mathbf{x}'\beta + \mathbf{z}'(t)\gamma] \quad [1]$$

where  $\lambda_0(t)$  = baseline hazard function,  $\mathbf{x}$  = vector of time-independent covariates,  $\mathbf{z}$  = vector of time-dependent covariates, and  $\beta$  and  $\gamma$  = vectors of corresponding regression coefficients.

The objective of the study was to compare the hazard of a sick cow with the hazard of a healthy cow within the same stage of lactation (i.e., within intervals for which the proportional hazards assumption is true). To compare the hazards of a cow or of several cows at different time points, the estimates of all time-dependent covariates should be combined with the values of the baseline hazard function at these time points. Otherwise, erroneous conclusions could be drawn. The study of Gröhn et al. (11) illustrated and discussed this problem.

How well the fit of a model improved when new terms were added to it was assessed by looking at the changes in  $-2 \log$  likelihood ( $-2\text{LOGL}$ ). Under a null hypothesis (i.e., no improvement of the fit), this likelihood ratio statistic follows a chi-square distribution with as many degrees of freedom as the number of estimable parameters added to the model. For example, the necessity to account for the interaction of disease and the period when disease occurs can be assessed by comparing the log-likelihood values of a model with disease only (reduced model) and a model with a term for the interaction of disease and period of occurrence (complete model). Similarly, the need for an extra interaction term with stage of lactation, during which the effect on culling is observed, can be assessed by comparing the log-likelihood values of the previous complete model, which becomes the reduced model, and a model in which a term for the three-way interaction of disease, period of occurrence, and stage of lactation has been added (complete model).

Five models were fitted; parity and calving season were covariates in all models. Model 1 contained terms for the interaction of disease and stage of lactation as defined previously. Model 2 contained terms for the interaction of disease and stage of lactation

and terms for current milk yield. All terms were time-dependent covariates. Model 3 contained terms for the interaction of disease and stage of lactation and a term for conception status. All terms were time-dependent covariates. Model 4 contained terms for current milk yield and conception status. Model 5 contained terms for the interaction of disease and stage of lactation and terms for current milk yield and conception status. The comparison of the effects of diseases alone (Model 1) with the effects of diseases adjusted for milk yield (Model 2), diseases adjusted for conception status (Model 3), and diseases adjusted for both milk yield and conception status (Model 5) was of interest. For completeness, results from Model 4 are also presented. Risk ratios (**RR**) and 95% confidence intervals were obtained for the covariates in each model; they measured the risk of being culled for a cow with a particular factor. All models were fitted using The Survival Kit of Ducrocq and Sölkner (8). Although some diseases did not have significant effects on culling at all stages of lactation, results are presented for all seven diseases of interest in this study.

## RESULTS

### Description of Data

The herds in this study were large; the median number of cows calving in 1994 in the study herds was 500 (range, 340 to 1037). Mean previous 305-d cumulative milk yield of the 14 herds in this study was 10,265 kg, which was higher than the mean for New York State (7528 kg). The overall annual culling rate in the 14 herds was 23.6%; many of these dairies were continuously expanding. Table 2 shows the overall lactational incidence risk, risks by parity, disease-specific culling risks, and day of culling by which 25% of the cows had been culled for each of the disorders; nearly two-thirds of the cows did not have any of the disorders listed.

### Goodness of Fit

To find the best model based on likelihood ratio tests, a model containing only the main effects of diseases was fitted as a preliminary step. This model considered diseases as time-dependent but without an interaction with stage of lactation. Next, we considered the stage of lactation in which culling occurred in addition to the period of occurrence of the diseases. We wanted to determine whether the interaction of stage of lactation and disease was important as was

TABLE 2. Lactational incidence risks, disease-specific risk of culling, and day by which 25% of the cows had been culled for each disease in 7523 Holstein dairy cows in New York State from calving in 1994 until September 30, 1995.

Disease	Incidence risk by lactation							Disease-specific culling risk <sup>1</sup>	25% of Cows were culled
	All	1	2	3	4	5	≥6		
	(%)								(d <sup>2</sup> )
Milk fever	0.9	0.1	0.4	0.7	3.1	4.0	6.1	47.1	168
Retained placenta	9.5	6.8	9.3	12.3	13.3	8.8	18.0	31.7	303
Displaced abomasum	5.3	5.5	4.6	6.4	6.0	4.3	3.1	26.9	359
Ketosis	5.0	4.2	3.9	6.0	8.3	6.1	7.7	32.5	295
Metritis	4.2	5.9	3.4	2.6	3.5	2.1	3.1	17.1	524
Ovarian cysts	10.6	11.2	11.5	9.1	10.3	7.3	8.0	20.9	491
Mastitis	14.5	11.5	13.8	16.7	20.1	20.1	19.9	32.7	283
No treatment	61.7	64.5	63.3	59.4	53.8	61.4	51.0	21.5	436

<sup>1</sup>Percentage of cows with a particular disease that was culled during lactation.

<sup>2</sup>Because the culling rate in the study period was approximately 25%, the values in this column refer to the day by which 25% of the cows had been culled for each disease.

suggested in our previous research (11). Results of this exercise are shown in Table 3; each disease was added separately to a model containing parity, milk yield, and conception status. When the  $-2\text{LOGL}$  values for each disease were compared, with and without an interaction with stage of lactation, only interactions of displaced abomasum, ketosis, mastitis (ovarian cysts were borderline), and stage of lactation were significant. However, for consistency, and because we determined that interactions of diseases and stage of lactation were important, interactions of stage of lactation and disease for all diseases were included in subsequent analyses. Finally, it was of interest to examine how milk yield and conception status changed the estimates of the effects of the interaction of disease and stage of lactation (Model 5). Because the results of this study indicated that

milk yield and conception status were important factors in culling, only results from Model 5 are presented in Table 4. Table 4 provides the  $-2\text{LOGL}$  values and their associated probabilities for each term in the most comprehensive model (Model 5) as well as nonsignificant effects. The full model and the full model without the term of interest were compared and provided an indication of how much more variation the term of interest explained. The covariate that best improved the fit of this model was conception status; the largest difference ( $-2\text{LOGL}$  per degree of freedom) was between the full model and the same model without conception status. Parity was also highly significant. Current milk yield and some of the diseases listed, particularly mastitis, also improved the model fit significantly.

TABLE 3. Comparison of likelihood of disease and interaction with stage of lactation for 7523 Holstein dairy cows in New York State that calved in 1994.

	No interaction				Interaction			
	$-2\text{LOGL}^1$	Change in $-2\text{LOGL}^2$	Change in df	$P > \chi^2$	$-2\text{LOGL}$	Change in $-2\text{LOGL}$	Change in df	$P > \chi^2$
Initial model <sup>3</sup>	18,789.9	...	...	...	18,789.9	...	...	...
Mastitis	18,713.2	76.7	4	0.0000	18,671.3	118.6	14	0.0000
Ketosis	18,780.2	9.7	1	0.0018	18,761.4	28.5	5	0.0000
Milk fever	18,778.6	11.3	1	0.0008	18,777.3	12.6	3	0.0055
Displaced abomasum	18,787.6	2.3	1	0.1297	18,771.2	18.7	6	0.0047
Ovarian cysts	18,788.7	1.2	2	0.5518	18,783.0	6.9	4	0.1428
Retained placenta	18,789.9	0.0	1	0.9687	18,788.6	1.3	3	0.7203
Metritis	18,789.9	0.0	1	0.8271	18,789.6	0.3	3	0.9530

<sup>1</sup> $-2$  Log likelihood; values are rounded to nearest decimal place.

<sup>2</sup>Change in the  $-2\text{LOGL}$  that resulted from adding the term to a model containing parity, milk yield, and conception status; values are rounded to nearest decimal place.

<sup>3</sup>Model contained parity, milk yield, and conception status.

TABLE 4. Comparison of likelihoods for terms in Model 5 for 7523 Holstein cows in New York State that calved in 1994.

Covariate	-2LOGL (Last) <sup>1</sup>	Change in df	Change in -2LOGL <sup>2</sup>	Change in -2LOGL per change in df	<i>P</i> > $\chi^2$
All <sup>3</sup>	18,610.4	. . .	. . .	. . .	. . .
Conception status	19,492.1	1	881.7	881.7	0.0000
Parity	18,960.7	5	350.3	70.1	0.0000
Current milk yield <sup>4</sup>	19,676.6	30	1066.2	35.5	0.0000
Mastitis	18,728.5	14	118.1	8.4	0.0000
Ketosis	18,632.1	5	21.7	4.3	0.0006
Milk fever	18,621.3	3	10.9	3.6	0.0124
Displaced abomasum	18,623.2	6	12.8	2.1	0.0453
Ovarian cysts	18,617.6	4	7.2	1.8	0.1271
Retained placenta	18,611.2	3	0.8	0.3	0.8463
Metritis	18,610.9	3	0.5	0.2	0.9093

<sup>1</sup>-2 Log likelihood; -2LOGL that resulted from adding the term to the model last, independently of the other terms; values are rounded to nearest decimal place.

<sup>2</sup>Difference in -2LOGL between model for specific covariate and model on top line (containing all terms); values are rounded to nearest decimal place.

<sup>3</sup>Model containing all of the terms listed subsequently (conception status through metritis).

<sup>4</sup>Test day milk yield. Milk yield intervals are given in Table 5.

### Effect of Diseases on Culling

Tables 5 through 8 show the factors that were associated with culling in Models 1 through 5. Older cows were much more likely to be culled (Table 5). Calving season was not a risk factor for culling (results not shown). During the 1st mo of lactation, first parity cows were more likely to be culled (Models 2, 4, and 5) than were older cows (Table 5). Estimates for current milk yield were fairly consistent across models, except that RR for cows missing test day values differed somewhat (Table 5). Cows missing test day yields in the early and middle stages of the current lactation were at an extremely high risk of culling. Higher milk yield on a particular test day was protective against culling, especially later in lactation, compared with mean milk yield. On a given day, a cow that had not yet conceived was more than seven times as likely to be culled, regardless of the model considered (Table 6).

Because we determined that interactions of disease and stage of lactation were important, all results pertaining to the effect of diseases on culling accounted for these interactions. The estimated RR presented in Tables 6 through 8 for diseases are not comparable when different stages of lactation are considered (11). These RR provide an indication of the risk that a diseased cow would be culled compared with the risk that a cow without that particular disease would be culled on the same day. Apparently, cows with milk fever (Table 6) or displaced abomasum (Table 7) were more than twice as likely to be culled than were healthy cows. Cows with retained placenta were more likely to be culled in later lacta-

tion than were cows without retained placenta (Table 6). Ketotic cows were more likely to be culled throughout lactation than were nonketotic cows (Table 7). The effect of ovarian cysts on culling differed depending on whether an adjustment was made for conception status (Table 7). Mastitis was an important risk factor throughout lactation (Table 8).

The effect of some diseases did not vary among models (i.e., whether or not current milk yield or conception status appeared in the model). In particular, this lack of difference was the case for displaced abomasum (Table 7) and for milk fever (Table 6) and ketosis (Table 7) in early lactation. However, the effect of the latter two diseases was different in late lactation when adjustment was made for conception status (Models 3 and 5): the RR increased from 1.6 to 2.3 for milk fever and decreased from 2.0 to 1.5 for ketosis. Retained placenta was a risk factor in Model 1 but not in any other model. Ovarian cysts were a factor in Models 1 and 2 in which they raised the risk of culling in late lactation, but, in Model 3, ovarian cysts decreased the risk of culling (Table 7). The RR for mastitis were higher in Model 1 than in Models 2, 3, and 5 (Table 8). The disease estimates in Model 1 were generally higher than those in the other models, which were adjusted for milk yield and conception status (Tables 6 through 8).

## DISCUSSION

### Likelihood Ratio Tests

By comparing likelihood ratios, the goodness-of-fit of a model can be determined. Table 3 indicates

TABLE 5. Risk ratios (RR) and 95% confidence intervals (CI) for parity and milk yield (previous 305-d milk yield and milk yield at 30, 60, 120, 180, and 240 d of current lactation) in the final Cox proportional hazards models for culling in a study of 7523 Holstein dairy cows in New York State from calving in 1994 until September 30, 1995.

Covariate	Model 1		Model 2		Model 3		Model 4		Model 5	
	RR	95% CI								
Parity										
1	1.0	...	1.0	...	1.0	...	1.0	...	1.0	...
2	1.6***	1.4–1.8	1.9***	1.6–2.2	1.6***	1.4–1.8	1.8***	1.5–2.1	1.8***	1.5–2.1
3	2.6***	2.3–3.0	3.1***	2.7–3.7	2.4***	2.1–2.8	2.9***	2.5–3.4	2.8***	2.4–3.3
4	3.1***	2.6–3.6	3.9***	3.3–4.6	2.8***	2.4–3.3	3.5***	3.0–4.2	3.3***	2.8–4.0
5	4.2***	3.4–5.1	5.2***	4.3–6.5	3.5***	2.9–4.2	4.4***	3.6–5.4	4.2***	3.4–5.2
≥6	4.7***	3.8–5.8	6.2***	4.9–7.7	3.8***	3.1–4.7	5.1***	4.1–6.4	4.7***	3.8–5.9
Current milk yield										
Previous 305-d yield										
(value for first 30 d)										
Parity 1										
Parity ≥2 (missing) <sup>1</sup>	...	...	1.9***	1.3–2.7	...	...	1.7**	1.2–2.4	1.7**	1.2–2.4
≤8577 kg	...	...	0.4	0.1–1.6	...	...	0.4	0.1–1.6	0.4	0.1–1.6
8578–10,073 kg	...	...	1.2	0.9–1.8	...	...	1.3	0.9–1.8	1.2	0.9–1.8
10,074–11,146 kg	...	...	0.9	0.6–1.3	...	...	0.9	0.6–1.4	0.9	0.6–1.3
11,147–12,332 kg	...	...	1.0	...	...	...	1.0	...	1.0	...
>12,332 kg	...	...	0.8	0.5–1.1	...	...	0.8	0.5–1.2	0.8	0.5–1.1
30 d										
Missing	...	...	1.1	0.8–1.6	...	...	1.1	0.8–1.6	1.1	0.8–1.6
≤29 kg	...	...	22***	9.0–55	...	...	22***	9.1–55	22***	9.1–55
30–34 kg	...	...	2.6	0.9–7.3	...	...	2.5	0.9–7.2	2.6	0.9–7.3
35–41 kg	...	...	1.0	...	...	...	1.0	...	1.0	...
42–47 kg	...	...	1.9	0.6–5.7	...	...	1.9	0.6–5.6	1.9	0.6–5.7
>47 kg	...	...	1.5	0.5–4.7	...	...	1.5	0.5–4.6	1.5	0.5–4.7
60 d										
Missing	...	...	47***	16–145	...	...	57***	19–168	40***	13–122
≤31 kg	...	...	7.2***	4.3–12	...	...	7.5***	4.5–13	7.1***	4.2–12
32–37 kg	...	...	1.2	0.6–2.3	...	...	1.2	0.6–2.4	1.2	0.6–2.3
38–42 kg	...	...	1.0	...	...	...	1.0	...	1.0	...
43–48 kg	...	...	1.3	0.7–2.4	...	...	1.2	0.7–2.4	1.2	0.6–2.4
>48 kg	...	...	0.8	0.4–1.7	...	...	0.8	0.4–1.6	0.8	0.4–1.6
120 d										
Missing	...	...	23***	8.8–59	...	...	19***	7.7–48	12***	4.6–31
≤31 kg	...	...	4.7***	3.1–7.1	...	...	4.3***	2.9–6.6	4.1***	2.7–6.3
32–36 kg	...	...	1.5	0.9–2.4	...	...	1.6	1.0–2.5	1.5	0.9–2.4
37–40 kg	...	...	1.0	...	...	...	1.0	...	1.0	...
41–45 kg	...	...	0.8	0.4–1.4	...	...	0.7	0.4–1.3	0.8	0.4–1.3
>45 kg	...	...	0.5*	0.2–0.9	...	...	0.5*	0.2–0.9	0.5*	0.2–0.9
180 d										
Missing	...	...	10***	3.5–29	...	...	8.9***	3.2–25	7.2***	2.5–20
≤30 kg	...	...	8.1**	5.0–13	...	...	7.3***	4.5–12	7.2***	4.4–12
31–34 kg	...	...	2.1**	1.2–3.6	...	...	1.9*	1.1–3.2	1.8*	1.1–3.2
35–37 kg	...	...	1.0	...	...	...	1.0	...	1.0	...
38–42 kg	...	...	0.8	0.4–1.6	...	...	0.8	0.4–1.5	0.8	0.4–1.5
>42 kg	...	...	0.6	0.3–1.2	...	...	0.6	0.3–1.2	0.6	0.3–1.2
240 d										
Missing	...	...	4.2**	1.7–10	...	...	7.3***	2.9–18	7.4***	3.0–19
≤24 kg	...	...	3.7***	2.9–4.6	...	...	4.2***	3.3–5.3	4.3***	3.4–5.5
25–29 kg	...	...	1.3	1.0–1.7	...	...	1.4*	1.1–1.8	1.5**	1.1–1.9
30–33 kg	...	...	1.0	...	...	...	1.0	...	1.0	...
34–37 kg	...	...	0.7**	0.5–0.9	...	...	0.8	0.6–1.0	0.8	0.6–1.1
>37 kg	...	...	0.5***	0.4–0.7	...	...	0.5***	0.4–0.7	0.5***	0.4–0.7

<sup>1</sup>Cows still in herd but missing a milk yield measurement.

\* $P < 0.05$ .

\*\* $P < 0.01$ .

\*\*\* $P < 0.001$ .

whether interactions of diseases and stages of lactation were important. The improvement in fit was greater when these interactions were considered; for displaced abomasum, the inclusion of this interaction caused the term to become significant. However, when the  $-2\text{LOGL}$  value for each disease was compared, with and without the interaction with stage of lactation, the improvement in fit was significant only for displaced abomasum, ketosis, and mastitis (ovarian cysts were borderline). For consistency, interactions for all seven diseases were included in subsequent analyses. Also, because it is more realistic to consider interactions of disease and stages of lactation when studying the effect of diseases on culling, such interactions were considered important.

From the results of the most complete model (Model 5; Table 4), conception status was the most important covariate, causing the largest increase in values for  $-2\text{LOGL}$  per degree of freedom. Parity and current milk yield were also very important covariates. Several diseases, particularly mastitis, also resulted in large increases in  $-2\text{LOGL}$  per degree of freedom.

Determining the best model is not only a statistical problem. If the primary interest is the overall effect of diseases on culling, then intervening variables, such

as milk yield and conception status, ought not be included in the model, whether or not they are significant. However, if the primary interest is how diseases directly affect culling, then such intervening variables ought to be included.

### Effect of Diseases on Culling

To maximize the profits in their enterprise, dairy farmers must make decisions about which cows to keep in the milking herd and which to sell. Culling decisions are based on several factors including disease, milk yield, conception status, parity, and stage of lactation. The main interest of this study was to determine the effects of several diseases on culling; these effects were both direct and indirect. Indirect effects of diseases may be mediated by milk yield. Also, pregnant and open cows are culled differently.

In all models, cows with milk fever were more likely to be culled during the first 30 d of lactation than were cows without milk fever (Table 6). Milk fever also increased the risk of culling during late lactation (after 240 d) in all models. However, the effect was significant only in Models 3 and 5. Dohoo and Martin (7) and Milian-Suazo et al. (16) found that milk fever increased the risk of culling, espe-

TABLE 6. Risk ratios (RR) and 95% confidence intervals (CI) for conception status, milk fever, and retained placenta in the final Cox proportional hazards models for culling in a study of 7523 Holstein dairy cows in New York State from calving in 1994 until September 30, 1995.

Covariate	Model 1		Model 2		Model 3		Model 4		Model 5	
	RR	95% CI								
Conception status										
Before conception	...	...	...	...	7.4***	6.5–8.5	7.5***	6.6–8.6	7.5***	6.5–8.6
After conception	...	...	...	...	1.0	...	1.0	...	1.0	...
Milk fever <sup>1</sup>										
No milk fever	1.0	...	1.0	...	1.0	...	...	...	1.0	...
Period and stage of lactation										
1, 1	2.1*	1.1–3.9	2.2*	1.2–4.3	2.2*	1.1–4.1	...	...	2.3*	1.2–4.5
1, 2	1.3	0.7–2.2	1.3	0.7–2.3	1.3	0.7–2.3	...	...	1.5	0.8–2.6
1, 3	1.6	0.8–3.0	1.4	0.7–2.7	2.3**	1.2–4.5	...	...	2.1*	1.1–4.0
Retained placenta										
No retained placenta	1.0	...	1.0	...	1.0	...	...	...	1.0	...
Period and stage of lactation										
1, 1	1.1	0.8–1.5	1.1	0.8–1.5	1.1	0.8–1.5	...	...	1.1	0.8–1.6
1, 2	1.3*	1.0–1.6	1.0	0.8–1.3	1.2	0.9–1.4	...	...	1.0	0.8–1.2
1, 3	1.2	0.9–1.5	1.1	0.9–1.4	1.0	0.7–1.2	...	...	0.9	0.7–1.2

<sup>1</sup>The effect of a disease during a particular stage of lactation (see Table 1 for period in which disease occurred and stage of lactation when culling hazard was observed) is denoted as follows: i, j = effect of disease occurring in period i on culling observed in stage of lactation j. All effects are to be compared with the baseline condition of no disease.

\* $P < 0.05$ .

\*\* $P < 0.01$ .

\*\*\* $P < 0.001$ .

cially when the cow was also down. However, Bigras-Poulin (3) found the opposite effect; milk fever lowered the risk of culling by half.

Retained placenta had no effect on culling, except in Model 1 in which the risk of culling was increased between 31 and 240 d (Table 6). This result suggests that the milk yield and the conception status of a cow with retained placenta act as intervening variables in the effect of this disease on culling. Oltenacu et al. (18) found that retained placenta increased the risk of culling, but Beaudeau et al. (1) found that retained placenta was protective against culling, at least during first lactation.

Displaced abomasum was a risk factor for culling in early lactation (1 to 30 d). Displaced abomasum was not a factor in culling later in lactation in any

model (Table 7). Culling for displaced abomasum appeared to be independent of culling for milk yield and conception status. Milian-Suazo et al. (17) found that left displaced abomasum was associated with culling. In contrast, Cobo-Abreu et al. (4), Martin et al. (14), and Dohoo and Martin (7) found no association between abomasal displacement and culling.

In this study, cows with ketosis were more likely to be culled soon after diagnosis than were cows without ketosis; ketosis also had an effect on culling later in lactation (Table 7). The effects of ketosis within each stage of lactation were generally consistent among models, even after adjustment for milk yield and conception status. One exception was noted after 240 d, when conception status was considered (Models 3 and 5). One possible interpretation is that ketosis

TABLE 7. Risk ratios (RR) and 95% confidence intervals (CI) for displaced abomasum, ketosis, metritis, and ovarian cysts in the final Cox proportional hazards models for culling in a study of 7523 Holstein dairy cows in New York State from calving in 1994 until September 30, 1995.

Covariate	Model 1		Model 2		Model 3		Model 4		Model 5	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Displaced abomasum <sup>1</sup>										
No displaced abomasum	1.0	...	1.0	...	1.0	...	...	...	1.0	...
Period and stage of lactation										
1, 1	2.4***	1.5-3.8	2.4***	1.5-3.7	2.4***	1.5-3.7	...	...	2.3***	1.5-3.6
1, 2	1.5	0.8-3.0	0.7	0.4-1.4	1.5	0.8-3.0	...	...	0.7	0.4-1.4
1, 3	1.1	0.6-2.2	0.8	0.4-1.6	1.1	0.6-2.1	...	...	0.8	0.4-1.6
1, 4	0.9	0.5-1.6	1.0	0.5-1.8	0.9	0.5-1.6	...	...	0.9	0.5-1.7
1, 5	1.3	0.7-2.3	1.1	0.6-2.0	1.1	0.6-2.0	...	...	1.0	0.5-1.7
1, 6	1.0	0.7-1.4	1.1	0.8-1.5	1.1	0.7-1.5	...	...	1.1	0.8-1.6
Ketosis										
No ketosis	1.0	...	1.0	...	1.0	...	...	...	1.0	...
Period and stage of lactation										
1, 1	1.9*	1.2-3.0	1.9**	1.2-3.1	1.9**	1.2-3.0	...	...	1.9**	1.2-3.1
1, 2	1.2	0.7-2.0	1.0	0.6-1.7	1.2	0.7-2.0	...	...	1.0	0.6-1.7
1, 3	2.0**	1.2-3.4	1.9*	1.1-3.1	1.9**	1.2-3.2	...	...	1.7*	1.0-2.8
1, 4	0.7	0.4-1.4	0.7	0.4-1.3	0.7	0.4-1.3	...	...	0.6	0.3-1.1
1, 5	2.0***	1.4-2.7	2.1***	1.5-2.9	1.5*	1.1-2.0	...	...	1.6**	1.2-2.3
Metritis										
No metritis	1.0	...	1.0	...	1.0	...	...	...	1.0	...
1, 1	1.2	0.7-2.0	1.0	0.6-1.7	1.1	0.7-1.9	...	...	1.0	0.6-1.7
1, 2	0.9	0.5-1.4	1.0	0.6-1.6	0.8	0.5-1.3	...	...	0.8	0.5-1.4
1, 3	1.0	0.6-1.5	0.9	0.6-1.4	1.0	0.6-1.5	...	...	0.9	0.6-1.5
Ovarian cysts										
No ovarian cysts	1.0	...	1.0	...	1.0	...	...	...	1.0	...
Period and stage of lactation										
1, 2	0.9	0.6-1.2	1.0	0.7-1.4	0.6*	0.5-0.9	...	...	0.7	0.5-1.1
1, 3	1.1	0.8-1.5	1.3	1.0-1.8	0.9	0.6-1.2	...	...	1.1	0.8-1.5
2, 2	1.0	0.6-1.8	1.2	0.7-2.1	0.6*	0.3-1.0	...	...	0.6	0.4-1.1
2, 3	1.4*	1.1-1.9	1.9***	1.4-2.5	0.8	0.6-1.1	...	...	1.0	0.7-1.3

<sup>1</sup>The effect of a disease during a particular stage of lactation (see Table 1 for period in which disease occurred and stage of lactation when culling hazard was observed) is denoted as follows: i, j = effect of disease occurring in period i on culling observed in stage of lactation j. All effects are to be compared with the baseline condition of no disease.

\* $P < 0.05$ .

\*\* $P < 0.01$ .

\*\*\* $P < 0.001$ .

delays conception, either because breeding of the ketotic cow is delayed or because fertility is decreased. When conception is not taken into account, the higher culling risk for open ketotic cows is attributed entirely to ketosis. When conception status is included, the direct effect of ketosis is reduced. Milian-Suazo et al. (16) found that ketosis increased the risk of culling. Beaudeau et al. (1) found that ketotic cows in parity 1 or 2 had nearly twice the risk of culling as did their nonketotic herd mates. Other studies (12, 18) have found that ketosis decreases the risk of culling.

Metritis had no effect on the risk of culling in this study. In contrast, some studies (4, 16, 18) found that metritis increased the risk of culling. Beaudeau et al. (1) found that metritis diagnosed after 50 d was a risk factor for culling. Dohoo and Martin (7) found that metritis decreased the risk of culling. This association probably occurred because cows with metritis were treated, but other cows, potentially with undetected metritis, were not treated and may have had lower fertility.

When adjustment was made for milk yield only (Model 2; Table 7), the hazard ratios for ovarian cysts were slightly higher than those in Model 1. In late lactation, all cows yield less milk, and those with ovarian cysts were more likely to be culled (Model 2).

When no adjustment was made for conception status (Models 1 and 2), cows with ovarian cysts after 120 d were more likely to be culled after 240 d than were cows without ovarian cysts. However, when adjustment was made for conception status (Models 3 and 5), ovarian cysts were no longer a risk factor for culling. Ovarian cysts act on culling mainly through delayed conception. When adjustments were made for both milk yield and conception status (Model 5), ovarian cysts had no effect on culling. Cows with ovarian cysts have longer days open (9). Bigras-Poulin (3), Milian-Suazo et al. (16), and Oltenacu et al. (18) found an increased risk of culling among cows with ovarian cysts.

In this study, mastitis appeared to be the disease that most influenced culling. For cows with mastitis between 1 and 60 d, the effect of the disease on culling during the first stage of lactation was constant across models (RR = 1.9; Table 8). During the second stage of lactation for these same cows, the consideration of conception status as well as disease (Model 3) did not change the effect of mastitis on culling, but the consideration of milk yield as well as disease did change the effect (Models 1 and 3, RR = 2.5; Models 2 and 5, RR = 1.6). The effect of mastitis was still great, but the effect was no longer as important when milk yield was included in the model. This finding

TABLE 8. Risk ratios (RR) and 95% confidence intervals (CI) for mastitis in the final Cox proportional hazards models for culling in a study of 7523 Holstein dairy cows in New York State from calving in 1994 until September 30, 1995.

Covariate	Model 1		Model 2		Model 3		Model 4		Model 5	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Mastitis <sup>1</sup>										
No mastitis	1.0	...	1.0	...	1.0	...	...	...	1.0	...
Period and stage of lactation										
1, 1	1.9***	1.3-2.8	1.9***	1.3-2.8	1.9***	1.3-2.8	...	...	1.9***	1.3-2.8
1, 2	2.5***	1.6-3.9	1.6	1.0-2.5	2.5***	1.6-3.9	...	...	1.6	1.0-2.5
1, 3	4.0***	2.7-5.7	2.7***	1.8-3.9	3.7***	2.6-5.4	...	...	2.5***	1.7-3.6
2, 3	7.3***	4.0-13	6.8***	3.7-13	6.6***	3.6-12	...	...	6.5***	3.5-12
1, 4	3.0***	2.0-4.3	2.4***	1.6-3.4	2.8***	1.9-4.1	...	...	2.2***	1.5-3.2
2, 4	3.9***	2.5-6.2	3.2***	2.0-5.1	3.6***	2.3-5.6	...	...	3.0***	1.9-4.8
3, 4	3.4	0.8-14	4.0	1.0-17	2.4	0.6-9.9	...	...	2.7	0.6-11
1, 5	2.2***	1.4-3.3	2.0***	1.3-3.0	1.9**	1.3-2.8	...	...	1.7*	1.1-2.6
2, 5	2.2**	1.3-3.9	1.8*	1.0-3.1	2.1**	1.2-3.7	...	...	2.0*	1.1-3.4
3, 5	4.9***	3.0-8.0	4.4***	2.7-7.3	4.0***	2.4-6.6	...	...	3.6***	2.2-6.0
1, 6	1.2	0.9-1.7	1.2	0.9-1.7	1.1	0.8-1.5	...	...	1.2	0.8-1.6
2, 6	1.1	0.7-1.7	1.0	0.6-1.5	1.1	0.7-1.6	...	...	1.0	0.6-1.5
3, 6	1.5*	1.1-2.2	1.4	1.0-2.0	1.3	0.9-1.9	...	...	1.2	0.8-1.7
4, 6	2.7***	1.5-4.6	2.7***	1.6-4.8	2.6***	1.5-4.6	...	...	2.7***	1.5-4.9

<sup>1</sup>The effect of mastitis during a particular stage of lactation (see Table 1 for period in which mastitis occurred and stage of lactation when culling hazard was observed) is denoted as follows: i, j = effect of mastitis occurring in period i on culling observed in stage of lactation j. All effects are to be compared with the baseline condition of no mastitis.

\* $P < 0.05$ .

\*\* $P < 0.01$ .

\*\*\* $P < 0.001$ .

was generally true for all mastitic cows in all stages of lactation; the RR for mastitis decreased when milk yield was added to the model (Models 2 and 5). The addition of conception status to the model (Models 3 and 5) decreased the RR for mastitis in most cases. Beaudeau et al. (1) pooled data from several lactations and used similar methodology as was used in this study. Those researchers (1) found that mastitis was an important risk factor for culling among French Holsteins. Many other studies (7, 10, 11, 12) have also found that mastitis was an important risk factor for culling.

When results from different studies are being compared, several aspects should be kept in mind. The statistical methods used vary among studies as do the model variables; the inclusion of mediating factors, such as milk yield and reproductive performance, can alter the magnitude of the effect of some diseases on culling. Definitions of disease may vary. The number of observations analyzed also varies among studies; the exclusion of particular cows from the analysis (e.g., those with missing milk records) may alter the effect of some diseases on culling. Target populations and breeds of cows vary among studies. Culling policies of the herds in this study may differ greatly from those of herds in other studies. Most of these herds were almost always in some state of expansion. Finally, until recently, it has not been possible to account for time-dependence of certain covariates. The differences among studies just listed could lead to variation in results.

### Direct Versus Indirect Effects of Diseases on Culling

Model 1 in this study contained only the effects of parity and disease. Estimates for the effects of disease on culling in this model were, therefore, total (direct and indirect) effects; they were not adjusted for other factors such as milk yield or conception status. In their literature review, Beaudeau et al. (2) found that at least one-half of all cullings are primarily due to disease. However, the estimates for the effects of disease in Model 2 (and Model 5) indicated that dairy farmers also consider current milk yield in culling decisions. Most diseases cause a decline in milk yield; these decreases may be temporary (e.g., ketosis) (6), or longer lasting.

In this study, the estimates for some effects of disease changed when milk yield was also a covariate in the model. For example, the inclusion of current milk yield in general led to a substantial decrease of the effect of mastitis, but the estimates remained

large, which indicated that an indirect effect of mastitis on culling through reduced milk yield did exist but was not the only phenomenon involved in the culling process.

However, the way the effect of milk yield on culling was accounted for may be questioned. The test day milk yields in this study were interpolated from the nearest actual test day measurement. That is, not all cows had milk yield measured exactly on d 30, 60, 120, 180, and 240 of lactation. The values obtained may not reflect adequately the exact milk yield when culling occurred. Also, previous 305-d yield was considered only during the first 30 d of lactation; after 30 d, test day milk yields of the current lactation were considered.

In this study, cows missing milk weights on a particular day had a very high risk of culling. Some of these cows were culled shortly after this day, but the reason for culling is unknown. Although these estimates for missing milk weights do not provide much information regarding the effect of milk yield on culling, because they are fewer than 40 out of 7523, they do provide an interesting additional category of milk yields. Such cows are even more likely to be culled than are cows yielding milk in the lowest category on a particular test day. These cows were likely in the sick pen on the test day and thus did not have a recorded milk weight.

Results from Models 3 through 5 indicate that conception status is an important factor in culling decisions. In this study, conception status was set at time of conception. Although the dairy farmer did not have this information at that time, we decided that the time when he or she knew the conception status for certain was not critical. The effect of pregnancy on culling rate was large and would certainly be significant, regardless of the exact time of receiving this information. Most disease effects tended to decrease when conception status was included as a covariate. Some diseases, particularly reproductive diseases, affect conception (9). Open cows are more likely to be culled. Conversely, when a disease is diagnosed, the dairy farmer may decide not to breed that cow if he or she is planning to cull her anyway. However, in this study, it was not possible to distinguish between these two mechanisms. The distinction could be partly made using AI information: if a cow is bred at least once, it may be assumed that the absence of conception is not a consequence of the decision of the dairy farmer.

Another concern that this study was unable to address was what happened before the cow calved (i. e., previous disease history). Some cows may have

recently acquired some disease during the previous lactation or dry period, which, in addition to any current diseases, might have influenced the decision of the dairy farmer on how to handle these cows. Such a problem arises when cows are left censored; no information is known about them before they are entered into the study.

### Use of Time-Dependent Covariates

The appeal of the methodology used in this study is that, by using appropriate time-dependent covariates, the effect of diseases on the risk of culling can be determined at different stages of lactation. Results demonstrate that one overall measure of the effect of disease on culling is not sufficient. Indeed, previous studies (1, 11) have demonstrated the importance of time-dependent covariates in survival analysis; the effect of a covariate can be determined during different periods of interest, which is not possible when covariates are independent of time. The effect of covariates on the outcome is the same throughout the entire study period, which is not always the case, as with disease, milk yield, and conception status.

The caution required for the interpretation of the effects of disease when milk yield, conception status, or both are included illustrates one of the major difficulties associated with the use of time-dependent covariates. According to Kalbfleisch and Prentice (13), these covariates fall into two main classes. External covariates are not directly involved in the culling process. For example, herd, year, and calving season are covariates that do not change with the general health of the cow. In contrast, internal covariates are measurements taken on the individual cow and can be influenced by the failure mechanism. Their observed change with time contains information on the culling process. The inclusion of these covariates in the analysis provides useful information, but the results must be analyzed with great care. The analysis may show little or no difference between diseased and healthy cows if the effect of the disease is predominantly reflected through the change in covariates (e.g., through delayed conception).

### CONCLUSIONS

The results of this study suggest that diseases have an important effect on culling. Their effects differed depending on stage of lactation. Milk fever, retained placenta, displaced abomasum, ketosis, ovarian cysts, and mastitis all raised the risk of culling at certain stages of lactation; ovarian cysts were protective against culling when conception status was also con-

sidered. Mastitis, in particular, had an effect on culling throughout lactation. Metritis had no effect on culling. High milk yield was protective against culling. Cows that did not conceive had a significantly higher risk of culling than did cows that did conceive. The inclusion of conception status as a time-dependent covariate in the model changed the disease estimates somewhat, particularly those of ovarian cysts and milk fever and ketosis in late lactation. The effect of mastitis on culling was less, but not null, in models including current milk yield and conception status, which suggests that milk yield, conception status, and ovarian cysts and mastitis (and other diseases) are interrelated factors in their effect on culling. This research indicates that dairy farmers consider many factors, including diseases, milk yield, conception status, parity, and stage of lactation, when deciding whether and when to cull a cow.

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