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Evaluation of a contract breeding management program in selected Ohio dairy herds with event-time analysis II. Parametric frailty models

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Abstract

The effect of a contract breeding program offered by a breeding co-operative was assessed using parametric frailty models with event-time analysis technique in a field study of Ohio dairies. The program featured tail chalking and daily evaluation of cows for insemination by co-operative technicians; dairy employees no longer handled estrus detection activities. Test day records were obtained between early 2002 and mid-2004 for 16,453 lactations representing 11,398 cows in 31 herds identified as well-managed client herds by the breeding co-operative.

Various parametric distributions for event times available in a commercial software (Stata 9.1, College Station, TX) were tested to assess which distribution fit the calving-to-conception data best. After identifying the distribution with the best fit, a full model with potential confounders and other significant predictors of time to pregnancy was developed and then frailty terms were included in the model.

Generalized gamma and log-normal distributions fit the data best, but since gamma distribution does not allow the use of frailty effects, log-normal distribution was used in further modeling.

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Separate accelerated failure time models with frailty terms to account for latent effects at the herd, cow, or lactation level were developed, testing both gamma and inverse Gaussian frailty distributions. In these models, potential confounders and statistically significant predictors were also controlled for, and the association between the contract breeding program and the mean time to pregnancy was characterized using time ratios.

The log-normal model identified that interval to pregnancy was associated with breed, herd size, use of ovulation synchronization protocols, parity, calving season and somatic cell score (above or below 4.5) and maximum milk yield prior to pregnancy or censoring. While controlling for these factors, there was a reduction in average time to pregnancy among cows managed under the contract breeding program.

All frailty terms were highly significant, regardless of whether it was an individual frailty at the lactation level or a shared frailty at the cow or herd level, suggesting that there was considerable heterogeneity within these levels. Inclusion of a frailty term at the herd level changed the estimate for the contract breeding program considerably, while a frailty term on other levels did not, indicating that herd characteristics (e.g., overall management) have a substantial impact on reproductive performance and should be accounted for in the analysis. Interpretation using time ratios with or without a shared herd frailty found that the contract breeding program was associated with a reduction of 6.5% and 14.1% in mean time to pregnancy, respectively.

Keywords: Reproductive management; Tailhead chalking; Dairy; Event-time analysis; Frailty models; Log-normal distribution

1. Introduction

Inefficient detection of estrus is a significant problem in many modern dairy herds (Heuwieser et al., 1997; Rocha and Rocha, 2001). Over time, a number of aids have been developed to assist dairy producers in identifying cows for insemination, including pressure-sensitive heat mount detectors (Gwazdauskas et al., 1990; Williamson, 1975), tail paint and chalk marking (Kerr and McCaughey, 1984; Williamson, 1980), teaser animals with marking devices (Stevenson and Britt, 1977), pedometers (Kiddy, 1977; Peter and Bosu, 1986), radiotelemetric pressure sensing devices (At-Taras and Spahr, 2001; Dransfield et al., 1998), and pharmacologic synchronization of ovulation (OvSynch) using administration of gonadotropin releasing hormone and prostaglandin (Pursley et al., 1997).

A dairy breeding cooperative in Ohio has begun offering a contract breeding management program to its clients. This program, referred to as a full service technician program (FSTP), uses tailhead chalk or paint as an estrus detection aid. While tailhead marking is not a novel estrus detection aid, the salient feature of the FSTP program is that, on a daily basis, an artificial insemination (AI) technician visits the farm to assess chalk/paint marks to make an insemination decision.

Previously, Cox proportional hazards modeling techniques were used to estimate the association between the FSTP and reproductive efficiency (in terms of relative hazard of pregnancy) while controlling for other significant predictors (Meadows et al., 2006). It was concluded that cows managed under FSTP had a 30–40% increased hazard of pregnancy

compared to non-FSTP cows. This result was consistent between a fixed covariates only model (hazard ratio [HR] for FSTP cows 1.32) and a model that allowed time varying covariates (HR for FSTP cows 1.39).

In the prior analysis, some factors of interest with respect to reproduction were not measured or were unmeasurable in the study. These factors could be present at the herd level, such as nutrition, calving hygiene, and general ‘‘management capabilities’’. Alternatively, there were unmeasured factors at the cow level such as intrinsic fertility, and at the lactation level such as periparturient diseases. The use of ‘‘well-managed’’ herds as the study population was intended to reduce heterogeneity in these unmeasured factors. Based on the selection of the study herds and the use of analytic control of available measured factors, it was concluded that potential biases because of the effects of unmeasured information were minimized and the inferences acceptable (Meadows et al., 2006). However, these previous analyses were not able to adjust for the correlated data structure due to cows being clustered within herds and some cows contributing information from more than one lactation.

There is an analytical technique available for the analysis of event-time data that can account for effects of unmeasured, or latent, variables and/or for non-independence of observations. The shared frailty models for survival analysis are generalizations of standard survival models and are analogous to the correlated data and random effects models in linear regression (Gutierrez, 2002). An individual frailty model accounts for heterogeneity among individual units of observation, while the shared frailty model accounts for latent variables that operate at hierarchical levels above the unit of observation (Gutierrez, 2002). The unit of observation in this study was a single lactation within a cow, while higher levels of aggregation and shared frailty were at the cow and the herd level.

While semi-parametric (Eicker et al., 1996; Harman et al., 1996b,c; Lee et al., 1989; Suriyasathaporn et al., 1998) and parametric (Harman et al., 1996a) survival models have been described and used previously in the analysis of dairy reproductive performance, frailty models have been used only very recently. These have used either parametric (Schnier et al., 2004) or semiparametric baseline hazard functions (Maizon et al., 2004). Previous studies using parametric models with calving-to-conception data have used a Weibull distribution, assuming that fertility of cows increases steadily throughout the lactation (Harman et al., 1996a; Schnier et al., 2004). The observation period in the study of Schnier et al. (2004) started 30 days after calving and in the study of Harman et al. (1996a) 56 days post partum. However, if the observation period begins at calving, and a typical 45–60-day voluntary waiting period is applied before breeding of cows begins, the hazard of conception is practically zero at the beginning of the lactation. Additionally, as time passes and the most fertile cows have conceived, the population-at-risk that is left in the breeding pool, is typically composed of the ‘‘problem breeders’’ with lower fertility (Chebel et al., 2004). Thus, this would suggest that hazard of conception on a population level is not monotonically decreasing or increasing as a Weibull distribution assumes.

The objective of this analysis was to explore which parametric distribution would best fit the calving-to-conception data. Another objective was to develop and assess parametric survival models with frailty effects at different levels of organization (lactation, cow, or herd).

2. Materials and methods

Data for this study came from dairies that were clients of a single breeding co-operative. Of its 1700 herds client base in Ohio, the co-operative identified 42 ‘‘well-managed’’ herds to be targeted for inclusion in the study population. The study population included herds that managed their own estrus detection as well as a sample of the 90 client herds that participated in FSTP. Herd selection, contact, interviews, data acquisition, and preparation of data for analysis were discussed in detail previously (Meadows et al., 2006). The same dataset that was used in the prior fixed covariates model analysis was used in this study. Data were analyzed using Stata 9.1 (Stata Corporation, College Station, TX).

2.1. Background about frailty models

A straightforward way of thinking about individual frailty and shared frailty models is that they are survival models with an additional parameter estimated to represent unmeasured factors that cause the failure time for a subject or groups of subjects to deviate from the expectation of the population (Gutierrez, 2002). This frailty parameter is assumed to act multiplicatively on the population hazard function and is a random variable with mean 1 and some specified variance structure (Gutierrez, 2002). Being a multiplicative parameter, if an individual has frailty of 1, then there is no adjustment made to the population hazard function. Individuals with a frailty >1 have increased risk of experiencing the event; individuals with a frailty <1 have decreased risk of failure.

Although individual frailty and shared frailty models are extensions of standard survival analysis techniques, interpretation of model output for covariates has some important nuances. The proportional hazards context assumes that the HR estimate for a covariate does not change over time, and it is interpreted as a multiplicative change in the hazard of occurrence of the event when a particular covariate increases by 1 unit (Klein and Moeschberger, 2003). In individual and shared frailty models, the HR for a given covariate has a similar interpretation but with the very important qualifier that the HR is conditioned on the frailty, meaning that proportional hazards hold true over time only for subjects with identical frailty (Gutierrez, 2002). In the unconditional sense, the HR estimates for subjects with unequal frailty are generally valid at time 0 (Gutierrez, 2002). As time progresses, the effect of an individual’s frailty tends to dominate the population effect estimate. Thus, inferences from the HR obtained from frailty models should be done with caution, and are only valid in unique circumstances.

Interpretation of individual and shared frailty models can be made easier by using the accelerated failure time (AFT) metric (Gutierrez, 2002), which is possible when the baseline hazard function is parametrically defined. In the AFT metric, effects of covariates can be estimated using time ratios (TR) (Klein and Moeschberger, 2003). Time ratios are interpreted as the relative effect on the mean time to event; if $\mathrm{TR} < 1$, the covariate is associated with a shorter mean time to event (increased risk), while $\mathrm{TR} > 1$ suggests that the covariate is associated with a longer mean time to event (decreased risk) (Klein and Moeschberger, 2003). In frailty models analyzed in the AFT metric, the TR interpretation is the same in both the conditional and unconditional sense—the TR does not change over

time for subjects with unequal frailty (Gutierrez, 2002). Thus, TRs are excellent effect estimates that are easily generalized in AFT models that include frailty effects.

2.2. Parametric baseline hazard functions

Frailty effects can currently be incorporated in semiparametric proportional hazards (PH) models, but due to the limitations discussed above in interpretation of hazard ratios in frailty models, the analyses in this study were restricted only to parametric frailty models interpreted in AFT metric. Published studies using parametric models with dairy calving-to-conception data have used a Weibull distribution (Harman et al., 1996a; Schnier et al., 2004), but the fit of other distributions to these data have not been explored. Six different distributions were considered in this study for analyzing time-to-event data: exponential, Weibull, Gompertz, log-normal, log-logistic, and generalized gamma distribution. Exponential, Weibull, and Gompertz regressions can be interpreted in pH metric and exponential and Weibull models also in AFT metric. Log-normal, log-logistic, and generalized gamma regressions are only interpreted in AFT metric (Cleves et al., 2004).

The fit of each distribution to the current data was evaluated with a model with FSTP status as the only predictor using Akaike's information criteria (AIC) and the shape of the hazard curves. AIC penalizes each model's log likelihood ($\ln L$) to reflect the number of parameters being estimated. For the parametric survival models, AIC is defined as

$$\mathrm{AIC} = -2\ln L + 2(k + c)$$

where k is the number of model covariates and c is the number of model-specific distributional parameters (Cleves et al., 2004). While all the evaluated models had the same number of covariates (at this stage of modeling, only FSTP-status), the various distributions have different number of distributional parameters that are estimated during the modeling process, and thus AIC was used to assess the fit of the models instead of $\ln L$. Hazard curves for each distribution were graphed and both physiology and practical management aspects of dairy cow fertility and reproduction were considered when assessing the shape of the hazard curves and when deciding which distribution best fit the data.

2.3. Parametric model with no frailty effect

The parametric distribution with the most appropriate fit was chosen and a full model without any frailty term was developed. First, univariable parametric models were evaluated with FSTP status, breed, herd size classification, use of OvSynch protocol in herd, whether somatic cell score (SCS) ever exceeded 4.5 prior to pregnancy or censoring, parity, calving season, and maximum test day milk yield prior to pregnancy or censoring as predictors. Significance testing of these predictors was performed by using the Wald χ^2-test for covariates with 1 degree of freedom and likelihood ratio (LR) test for covariates with multiple degrees of freedom.

All predictors with P-value <0.20 were placed into a multivariable model and covariates were removed in a backwards elimination process using P-value >0.05 as reason for removal. One exception was that FSTP status was included in all multivariable

models, because the intent was to determine the relationship between FSTP status and time to pregnancy while controlling for other factors related to reproductive outcomes. The predicted hazard functions for FSTP and non-FSTP herds using the final model were also graphed.

2.4. Parametric model with frailty terms

Currently, software available for analyzing survival data have limitations such that, e.g., frailty terms can be introduced only as unique non-nested effects and inclusion of frailty effects within stratified analyses is not possible. Therefore, in analyzing these data separate models with frailty terms at three distinct levels of aggregation were evaluated: herd, cow, and lactation. The full model with the chosen parametric distribution without a frailty term was used as the starting model and an individual frailty or a shared frailty term was added one at a time. When using frailty effects, their distribution could be specified either as a gamma or inverse Gaussian structure (Cleves et al., 2004). Use of the gamma distribution allows the frailty component to completely dominate as time goes to infinity; with the inverse Gaussian distribution, the effect of other covariates diminishes, but never disappears completely (Gutierrez, 2002). The distribution of the frailty was chosen using the log-likelihoods; the model with the greater log-likelihood was chosen. Non-significant covariates were dropped from the model, if so indicated, using the procedure described above when developing the full model without frailties.

3. Results

3.1. Characteristics of study herds and cows

The dataset used in this analysis was the same as that used in the fixed covariates model described previously; results of data preparation and herd characteristics were described then (Meadows et al., 2006). The dataset for modeling had 16,453 lactations representing 11,398 cows from 31 herds. Of the 31 herds, 16 managed the reproductive program themselves and 15 were enrolled in FSTP. If a herd was enrolled in FSTP, all cows in the herd were managed under the program. There were 9978 lactations managed under FSTP; 63.2% of all cows had only one lactation, 31.7% had two lactations and 5.1% of the cows had records from three lactations included in the analyses.

3.2. Fit of different parametric event-time distributions to calving-to-conception data

Fit of the six different parametric distributions to the current calving-to-conception data was evaluated and the Akaike's information criteria from each model are presented in Table 1. The hazard functions from each event-time distribution are presented in Fig. 1. Based on the AIC's, the shape of the hazard functions and the knowledge about the dairy cow fertility and reproductive management in dairy herds, generalized gamma and log-normal distributions fit the data best. With both distributions, the hazard was zero in the beginning of the lactation (reflecting the voluntary waiting period), then increased up to

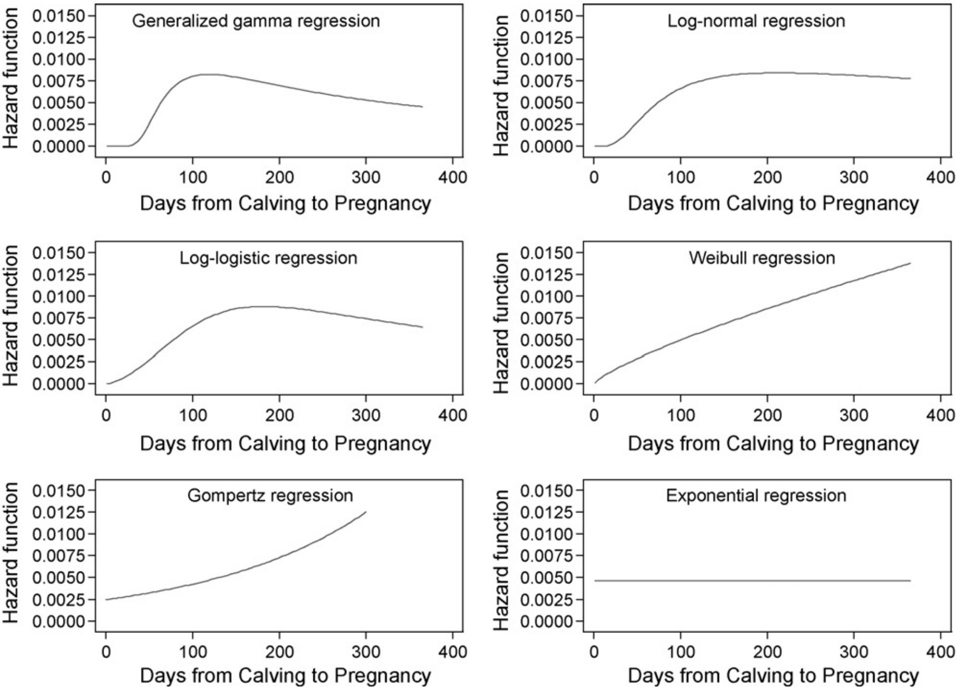

Fig. 1. Shape of the hazard functions using different parametric distributions for calving-to-conception interval.

100–120 days after calving and finally started declining towards the end of the lactation. The main difference between the distributions was that the hazard after 100 days in milk declined more rapidly using the generalized gamma than the log-normal distribution.

Currently, use of generalized gamma distribution does not allow for inclusion of shared frailty effects (Cleves et al., 2004) and because one of the objectives of the study was to adjust for unmeasured and/or unmeasurable (i.e., frailty) effects and to account for the correlated data structure due to cows being clustered within herds, log-normal distribution was used in all further analyses.

Table 1
Akaike's information criteria (AIC) for different parametric distributions for calving-to-conception data from models with the contract breeding program enrollment (FSTP) status as the only covariate

Distribution	AIC
Generalized gamma	28413.93
Log-normal	29005.37
Log-logistic	29651.29
Weibull	31138.45
Gompertz	33470.52
Exponential	35999.18

Table 2
Final accelerated failure time survival models for time to pregnancy using the log-normal distribution and various frailty effects: no frailty; shared herd frailty with a gamma distribution; shared cow frailty and individual lactation frailty with an inverse Gaussian distribution

Predictor	No frailty term		Herd-level frailty		Cow-level frailty		Lactation-level frailty	
	TR	95% CI	TR	95% CI	TR	95% CI	TR	95% CI
Full service technician program	0.859	0.840–0.878	0.935	0.906–0.965	0.865	0.846–0.885	0.873	0.854–0.892
Breed (Jersey vs. Holstein)	0.940	0.909–0.97	1.107	1.060–1.156	0.965	0.933–0.999	Not in the final model	
Herd size classification (relative to small herds)								
Medium (150–249 lactating cows)	0.901	0.871–0.934	0.844	0.841–0.929	0.894	0.862–0.926	0.897	0.868–0.927
Large (250 or more lactating cows)	0.862	0.834–0.892	0.937	0.894–0.982	0.860	0.831–0.889	0.869	0.842–0.897
Use of OvSynch in the herd	0.896	0.876–0.916	0.952	0.921–0.985	0.898	0.877–0.919	0.904	0.885–0.924
Somatic cell score ever exceeded 4.5	1.268	1.240–1.300	1.210	1.185–1.235	1.247	1.219–1.275	1.239	1.212–1.266
Parity (relative to first lactation)								
Second lactation	0.942	0.916–0.969	0.924	0.900–0.949	0.955	0.930–0.981	0.930	0.905–0.955
Third lactation	0.910	0.881–0.941	0.895	0.868–0.924	0.936	0.906–0.966	0.906	0.879–0.935
Fourth lactation	0.910	0.874–0.948	0.891	0.859–0.925	0.931	0.895–0.969	0.895	0.862–0.930
Fifth lactation or higher	0.975	0.934–1.018	0.946	0.910–1.982	0.989	0.947–1.032	0.945	0.908–0.984
Calving season (relative to winter)								
Spring (21 March–20 June)	1.121	1.086–1.157	1.087	1.057–1.118	1.113	1.079–1.148	1.109	1.076–1.142
Summer (21 June–20 September)	1.106	1.074–1.139	1.105	1.075–1.135	1.109	1.078–1.142	1.117	1.087–1.149
Autumn (21 September–20 December)	1.033	1.004–1.062	1.054	1.027–1.080	1.049	1.022–1.078	1.060	1.032–1.087
Maximum milk, per 10 kg	1.137	1.122–1.152	1.147	1.134–1.161	1.145	1.131–1.159	1.151	1.139–1.163
Variance estimates								
Sigma[a]	0.608	0.600–0.617	0.165	0.145–0.188	0.503	0.490–0.516	0.429	0.411–0.449
Theta[b]			3.730***	2.497–5.573	0.643***	0.523–0.761	1.446***	1.179–1.774

Time ratios (TR) less than 1 suggest a shorter time to pregnancy.

[a] Standard deviation of the log-normal distribution.

[b] Variance of the unobserved frailty parameter.

*** $P < 0.001$ for likelihood ratio test of H_0: theta = 0.

3.3. The results from the final models

Besides the FSTP status, the final model without a frailty term included breed, herd size classification, use of OvSynch protocol in herd, whether somatic cell score (SCS) ever exceeded 4.5 prior to pregnancy or censoring, parity, calving season, and maximum test day milk yield prior to pregnancy or censoring as predictors. The results are shown in Table 2 and they indicate that cows managed under the contract breeding program had 14.1% shorter time-to-pregnancy than cows in herds not enrolled in the program.

Graphs of the predicted hazard functions using the final model without a frailty term for FSTP and non-FSTP herds are presented in Fig. 2. The hazard of conception was close to zero until approximately 35 days after calving, it then started increasing in both groups, but more rapidly in the FSTP herds, indicating that hazard of conception was higher in the program herds than in the non-FSTP herds.

Frailty effects were highly significant ($P < 0.001$) at all levels (Table 2), suggesting that significant amount of heterogeneity existed at individual lactation as well as at cow and herd level. The inverse Gaussian was preferred over the gamma distribution as the lactation frailty (log likelihoods −12725.694 versus −12783.661, respectively) and as the shared cow frailty distribution (log L's −12738.158 versus −12760.632, respectively). The full model with inverse Gaussian shared herd frailty did not converge. The inverse Gaussian shared frailty at herd level was also tested using an empty model, a model with the FSTP status as the only covariate, with subsets of the data, and by setting the initial values for the evaluation from the shared herd gamma frailty model, but the initial log likelihood for inverse Gaussian herd frailty model could not be evaluated. Thus, only results from shared herd gamma frailty model were available. With individual inverse Gaussian frailty on

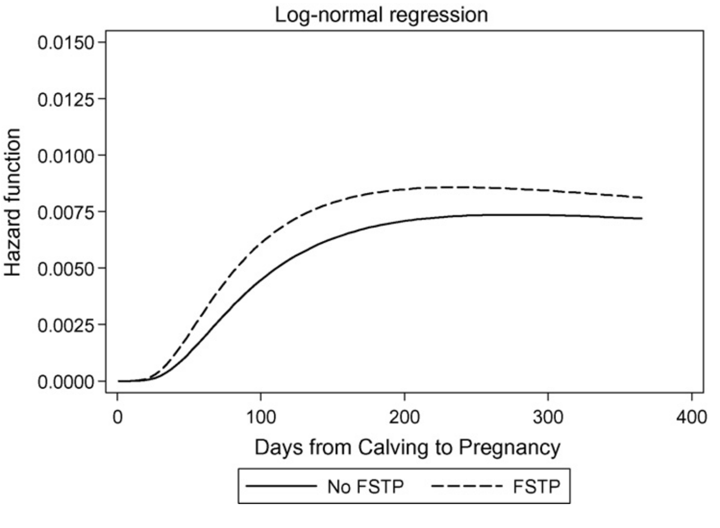

Fig. 2. Predicted hazard functions for herds enrolled in the FSTP and those not in the FSTP program from the final model without any frailty terms. Hazard curves are for first lactation Holstein cows that calved in winter, had somatic cell score below 4.5, produced an average peak milk yield and were in small herds that did not use hormonal estrus synchronization.

lactation level, breed of cows in a herd was not a significant factor anymore. Otherwise, the models with or without frailty effects (individual or shared) selected the same set of predictors and the results were similar between models. The only exception was that the breed effect was opposite between the herd shared frailty model and the rest of the models. Cows of Jersey breed had a shorter time to pregnancy in the no frailty model, but when herd level frailty was added to the model, Holstein cows appeared to have shorter time to pregnancy. Additionally and most importantly, when shared frailty effect was included at the herd level, the coefficient (and time ratio) for FSTP changed considerably (from −0.066 [TR = 0.86] to −0.152 [TR = 0.94]). This implies that herd acted as a confounder and while the effect of FSTP program was still beneficial and reduced the time to pregnancy when adjusting for the latent herd effect, its effect was not as strong as when unmeasurable herd effects were ignored (6.5% versus 14.1% reduction in time-to-pregnancy interval, respectively).

4. Discussion

As this was an observational study, the 31 herds studied here were not randomized to FSTP enrollment. This had the potential to introduce bias into the study if FSTP herds had systematic differences with the non-FSTP herds. Attempts were made to control for this by including herd characteristics such as use of OvSynch protocols and herd size indicator variables in the models. Additionally, cow-level covariates such as breed, and lactation level covariates such as parity, calving season, milk yield, and somatic cell score were adjusted for when indicated. Finally, the use of frailty models offered additional analytic control for differences between herds, cows, or lactations.

One objective of this study was to evaluate the fit of different parametric distributions to dairy calving-to-conception data. If based purely on statistical criteria (i.e., AIC), generalized gamma distribution fit the data best, but because the use of that distribution does not allow inclusion of shared frailty effects in the model (Cleves et al., 2004), the second best distribution, log-normal, was used in the modeling. The shape of the hazard function using generalized gamma, log-logistic and log-normal distributions suggested that hazard of conception in the beginning of lactation is zero, then increases and finally starts to decline towards the end of the lactation. On the other hand, Weibull and Gompertz distributions exhibited monotonously increasing hazard rates, and exponential distribution assumed a constant hazard; these are not realistic scenarios with respect to dairy cow fertility in true field conditions when modeling the time from calving to conception. In most US dairy herds, a 45–60-day voluntary waiting period is applied and breeding of cows begins only after that. Individual cows may be bred earlier if they exhibit strong signs of estrus. As lactation progresses, the population at risk contains cows that have problems conceiving (Chebel et al., 2004) and thus the population hazard appears to be declining (Allison, 1984). Therefore, when focusing on the population hazard (not individual cow hazard), it was not surprising that generalized gamma and log-normal fit the data best. The generalized gamma differed from the log-normal distribution mainly in that the hazard declined more rapidly after 100 days in milk. For an individual cow, log-normal distribution may, in fact, be more appropriate with much more subtle decline in hazard of

conception after 100 days. At this point of lactation, cows have passed the nadir of negative energy balance and the likelihood of them conceiving would not be expected to decline anymore (Butler, 2000).

The main objective of this study was to evaluate the association between the FSTP and the time to pregnancy using parametric frailty survival models, while identifying and controlling for potential confounding covariates. Although covariates identified in the final models were statistically significant, their numeric effects were relatively small and the nature of their measurements should be considered carefully before making any inferences. Pregnancy diagnosis was based on either a cow re-calving or on a veterinary diagnosis recorded in the records; in order to be considered pregnant in this study, a cow had to have been inseminated, successful fertilization was necessary, and pregnancy had to be maintained at least to diagnosis and in some cases to calving. Thus, any inferences need to consider the effect of a covariate on whether management would voluntarily delay insemination, as well as the effects on estrus expression, successful fertilization, and pregnancy maintenance to diagnosis.

Inferences from the AFT models with and without frailty terms developed in this study were similar to inferences made from the proportional hazards modeling. Factors that had $HR > 1$ in the proportional hazards model, such as FSTP use, breed, medium or large herdsize, use of OvSynch protocols, and parity greater than 1 had $TRs < 1$ in the AFT models. Likewise, factors that had $HR < 1$ in proportional hazards models, such as $SCS > 4.5$, calving season, and maximum milk yield, had $TR > 1$ in AFT models. Discussion of these effects was done in previous work with this dataset (Meadows et al., 2006). The effect of breed on the time to pregnancy unexpectedly changed when shared herd frailty was added to the model. Even though breed is a cow level trait, all herds included in this study were single breed herds and thus breed actually reflected a herd level effect. Without the shared herd frailty, Jersey cows had 6% shorter time to pregnancy than Holsteins. However, when the latent herd effects (such as nutrition, general management, etc.) were controlled for, Holstein cows had a shorter time to pregnancy than Jerseys. This would be in contrast to other studies (Washburn et al., 2002; White et al., 2002) which indicate that Jerseys have better fertility than Holsteins and may reflect the overall management in the herds enrolled in the current study.

Frailty terms were found to be highly significant at each level in the current analyses and the analyses showed slightly different results depending on whether frailty effects were used and at what level they acted. Use of an individual frailty term was supported by an argument that some important covariates (in this study, e.g., periparturient diseases) may have been ignored and that the unmeasured heterogeneity can be accounted for with an individual frailty effect (Gutierrez, 2002). Also, our earlier analysis with these same data suggested that most of the variability (78–90%) in calving-to-conception interval was on lactation level (Rajala-Schultz et al., 2006). This is in agreement with the results of Dohoo et al. (2001) who examined sources of variation in reproductive performance and concluded that 90% or more of the variability occurred at the lactation level. For these reasons, a model with individual frailty was evaluated to account for this heterogeneity. However, it is important to note that modeling individual frailty may also lead to bias (O'Quigley and Stare, 2002). O'Quigley and Stare (2002) demonstrated using their simulated data set with identical observations that individual frailty effect may appear

significant, even though no heterogeneity exists in the data. In the current study, estimates for all covariates in the model with an individual lactation frailty were very similar to those in the model without any frailty terms. This would imply that including an individual frailty may not be necessary.

Even though the cow level shared frailty was statistically significant, majority of the cows (>60%) had only 1 lactation during the study period which may have restricted the ability to evaluate the unmeasured cow level effects. On the other hand, compared to the non-frailty model and models with frailty at the cow or lactation level, the model with the shared frailty term at the herd level produced the greatest change in TR estimate for FSTP. This may suggest that unmeasured herd level effects confound the association between FSTP and time to pregnancy, and that frailty at the herd level is important. The variance of the herd level frailty was also numerically the largest. Until statistical software is further developed to allow shared frailty effects simultaneously at different levels of aggregation or to allow shared frailty terms in stratified analysis, these current analyses suggest that it is important to adjust for herd effects to minimize potential bias. A Dutch study reported that more variation in the occurrence of reproductive disorders (unmeasured factors in this study that the frailty models tried to adjust for) resided at the herd level than at the cow level (Klerx and Smolders, 1997). This further suggests that using the model with shared frailty at the herd level might be appropriate. Also, a recent frailty model effort used a herd-level frailty effect in modeling different reproductive outcomes (Maizon et al., 2004).

Overall, when evaluating the effect of the FSTP, the model without a frailty term and all three final frailty models arrived at similar conclusions. According to the model with no frailty effect, cows managed under FSTP had a 14.1% reduction in mean time to pregnancy. With a shared frailty at the herd level, cows in the FSTP herds had a 6.5% reduction in time to pregnancy. In the models with a shared cow-level frailty and an individual lactation frailty, cows managed under FSTP had 13.5% and 12.7% reduction in time to pregnancy, respectively. These results imply that the FSTP program was associated with significantly higher pregnancy rates and shorter calving intervals. Thus, the FSTP (or similar programs that increase estrus detection) improve reproductive performance which agrees with other recommendations (de Vries and Conlin, 2003; Stevenson et al., 1983).

5. Conclusions

The study described here assessed the fit of different parametric distributions to calving-to-conception data and evaluated the effects of a breeding program in which reproductive management was contracted out to breeding co-operative technicians. A parametric survival model with a log-normal distribution for event times with and without frailty terms identified a 6.5–14.1% shorter time to pregnancy for cows managed under the contract program, even while controlling for other significant predictors of fertility. Inclusion of a shared herd frailty in the model changed the effect of the breeding program, suggesting that herd acted as a confounder and that it is important to account for the unmeasured herd effects. While there were some differences in the effects of predictors in the frailty models, there was consistency in the effect of the contract breeding program, showing a reduction in time to pregnancy among cows in the program herds.

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